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AMERICAN
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CANCER COMPLICATING AND MODIFYING THE COURSE OF EPILEPSY.*

A REVIEW OF FIFTY-FIVE CASES.

BY MORGAN B. HODSKINS, M. D., AND RILEY H. GUTHRIE, M. D.,
Monson State Hospital, Palmer, Mass.

In a recent article [1] data were published which tended to minimize acidosis as an immediate factor in controlling convulsions, and which favored dehydration as a more valuable aid. It was shown, in support of dehydration, that epilepsy was relatively rare in three diseases in which body fluids were generally decreased, namely, diabetes mellitus, thrombo-angiitis obliterans and cretinism. Since it has been found by several investigators that cancer favors alkalosis of body tissues,[2, 3] 55 case records of untreated cancer complicating epilepsy have been reviewed in an effort to ascertain what influence this disease has upon the course of the seizures. Ordinarily alkalosis is associated with, or favors, hydration, but here we meet with a paradoxical situation in body chemistry, cachexia and dehydration associated with alkalosis, which is not met with in any other disease as far as the writers know. Assuming that untreated malignancy tends to induce a relative alkalosis, especially in its terminal stages, one logically would expect to find an increase in seizures in epileptics afflicted with cancer, if the shift in acid-base equilibrium influences convulsions as has been supposed. It has been observed in a few patients in the Monson State Hospital that alkalosis associated with malignancy does not increase the number of convulsions. During analysis of the cases, however, it became apparent that malignancy actually decreased the number of seizures.

*Read at the eighty-eighth annual meeting of The American Psychiatric Association, Section on Convulsive Disorders, Philadelphia, Pa., May 30, 1932.

Both the ketogenic diet [4, 5] and dehydration by fluid intake limitation [6] have been accepted as important methods in the treatment of epilepsy. A combination of these two methods has yielded most gratifying results in the hands of McQuarrie [7] and others, and at the same time has eliminated some of the unpleasant features and inconveniences of the ketogenic diet alone, or of dehydration by strict fluid intake limitation. Certainly, these methods have added materially to our therapeutic resources in the treatment of epilepsy but our interest in these methods extends far beyond their practical therapeutic results. Close analysis of the two methods reveals that they have many factors in common which may act in a synergistic manner. Hence, the logic of combining them. Acidosis induced by the ketogenic diet causes a negative water balance resulting in dehydration.[8] By reducing the carbohydrate intake one also reduces the demand for body fluids, releasing, to a considerable extent, body-bound water.

Geyelin,[9] Peterman,[10] and Wilder,[11] supporting the ketogenic diet, have attributed their favorable results to acidosis and to ketosis, or, indirectly, to an increase in the amount of calcium ion.[12] All these factors, it is claimed, decrease the irritability of the central nervous system. Fay [6] who advocates dehydration by the fluid limitation method, attributes his results to an alteration in intracranial hydraulics, lessening the liability to cerebral edema. But dehydration alone causes a shift of the acid-base equilibrium toward the acid side. That water metabolism plays an important rôle in physico-chemical processes is obvious because water is the medium in which occur all the chemical changes of the body. Another factor common to both methods, and the one which may explain their ameliorating influence, is an increase in the oxygen carrying capacity of the blood and an increase in dissociation of oxygen from hemoglobin. The findings which have been reported concerning the infrequency of epilepsy in conditions favoring dehydration,[1] and the decrease in frequency of seizures which has accompanied febrile disorders [13, 14] do not assist in clarifying the situation because in these conditions we may meet with both acidosis and dehydration. This state of affairs has led to considerable argument as to which is the more important factor in controlling convulsions, acidosis, or altered water metabolism.

Lennox [15] and others [16, 17] have shown that under normal conditions more oxygen is demanded by the brain than by other organs. That anoxemia favors the convulsive state is generally recognized, and that increased oxygen tension may relieve convulsions is quite generally accepted.[18] Indeed, administration of oxygen, both by the mask and intravenously, has afforded relief for epileptic patients.[19] Cobb and collaborators [20] have shown that increased oxygen tension is accompanied by vasodilation of the cerebral vessels, and that acidosis increases the dissociation of oxygen from hemoglobin, making more oxygen available for the tissues. Inhalation of an oxygen-carbon dioxide mixture causes dilatation of the cerebral vessels and elevation of systolic blood pressure, resulting in improved intracranial and, more especially, intracortical blood supply.[21] Cortical nerve tissue appears to be peculiarly sensitive to sudden decrease in oxygen tension and the normal function is especially dependent on the maintenance of constant and adequate oxygen supply. Landis [22] has shown that anoxemia increases the permeability of the capillaries to plasma proteins and permits water to pass through four times as fast as under normal conditions. Increase in capillary permeability may cause cerebral edema which is so frequently described in the acute convulsive state. Further studies in brain metabolism in epileptic patients may throw important light on this subject.

Favorable reports on the use of amyl nitrite in the acute convulsive state suggest that we are concerned with intracranial vascular conditions upon which depends the supply of nutrient to the nerve cells.[23] Caffeine, which causes a dilatation of cerebral vessels and favors an increase in the oxygen supply to the brain,[24, 25] has had a favorable influence on convulsions. In our experience caffeine-sodium benzoate, 15 gr. (1 gm.), daily, administered sub-cutaneously, has decreased the frequency of epileptic convulsions. The hypothesis that cerebral vaso-constriction is a precipitating factor in the acute convulsive state has been formulated.[1, 26] Many patients suffering from epilepsy and migraine present other evidences of autonomic imbalance. One is reminded of other autonomic phenomena occurring in equally dramatic situations, namely, the vaso-vagal attacks of Gowers, neurocirculatory asthenia, and vagotonic crises.[27] The character of these clinical syndromes lends weight to the concept that cerebral anoxemia, whether induced by angiospasm,

or by temporary circulatory collapse, deserves an important place in the physicochemistry of the acute convulsive state, and that vasodilation of the cerebral vessels with its subsequent increase in oxygen supply to the brain is, in some cases, an immediate factor in controlling convulsions.

The problem of muscle tone and its relation to oxygen metabolism is of extreme interest. The spectacular results of the direct administration of oxygen, and of the intravenous injection of sodium iso-amyl-ethyl barbiturate (amytal), in catatonia, speak for the profound influence of oxygen metabolism on human behavior and on muscle tone.[28] Our present knowledge of the clinical syndrome, angina pectoris, which may be caused by coronary spasm or sclerosis, and which is relieved by vasodilators, especially the nitrites, serves to emphasize the pernicious, if not actually fatal, effects of localized anoxemia. The cardiac spasm appears to be due to relative ischemia of the heart muscle incident to coronary narrowing and subsequent oxygen deficiency. Here, one is reminded that phenobarbital, which is an effective drug in the treatment of epilepsy, causes dilatation of cerebral vessels,[29] and sodium iso-amyl-ethyl-barbiturate (sodium amytal), which, in our experience has been most spectacular in relieving twelve patients of status epilepticus, probably acts in a similar manner. The favorable action of both these drugs in the treatment of epilepsy may be due, at least in part, to vasodilatation, thus facilitating oxygenation. In angina the vessel-spasm underlying heart-spasm appears to be a parallel process to cerebral angiospasm which may precipitate the epileptic seizure. Cardiac and visceral aura, so frequently described by epileptics, may represent component parts of the same angiospastic process which, if involving the vessels of the midbrain, causes temporary suspensions and sudden fluctuations in muscle tone. The view that thalamic processes add feeling-tone to sensation and that thalamic stimuli can be conditioned for certain patterns of neurone action may explain the familiarity of the aura in some epileptics and the constancy of the sequence of events. Theoretically, alkalosis, which is frequently associated with intracranial vasoconstrictor phenomena,[20, 21] may limit the supply of oxygen to the cerebrum, and acidosis which favors cerebral vasodilatation could exert a favorable influence upon seizures by improving the cerebral circulation. Cerebral symptoms

which have been observed in Raynaud's disease [33] illustrate the protean manifestations which may occur in vasomotor neurosis.[33]

It is not our purpose to reduce the study of etiologic factors in epilepsy to the vegetative level, but to emphasize the vasomotor component, and to attempt to correlate this with equally obscure physicochemical processes, especially water metabolism [34] and oxygen utilization. Without envisaging epilepsy in terms of biochemistry, one may see in it a plausible approach to the study both of individual predisposition, and of precipitating life situations which are so intimately associated with metabolic changes. Indeed, metabolic products, which accrue in intensely affective scenes, may damage, or render sensitive to damage, tissues, and progressively impair their integrity.[35] In untreated cancer patients one finds dehydration and increased metabolic activity apparently associated with a tendency toward alkalosis. Hyperglycemia, which is generally associated with cancer, may be a factor in influencing the convulsion threshold—a factor with which we are not prepared to deal.

The results of our review of the following 55 cases of cancer occurring in the course of pre-existing epilepsy tends to discredit alkalosis as an important factor in precipitating seizures and lends support to the belief that dilution of extracellular body fluids is a more essential factor in inducing seizures,[36, 37, 38] while dehydration, which inevitably occurs in the progress of this chronic disease, reduces the frequency of seizures. The records of 15 of these cases were obtained at the Monson State Hospital. Twenty case records were submitted by courtesy of Dr. G. G. Kineon, Superintendent, Ohio State Hospital for Epileptics, 15 by courtesy of Dr. William T. Shanahan, Superintendent, Craig Colony, New York, and four by courtesy of Dr. Dan S. Renner, Superintendent, Village for Epileptics, Skillman, New Jersey. Dr. W. A. Crooks, Superintendent, Michigan Farm Colony for Epileptics, has favored us with a report of one case (not included in table) of carcinoma of the breast in an epileptic woman in whom the number of seizures did decrease slightly over a period of five years, during which the malignancy was progressive, and during the last year of her life; however, she continued to have convulsions until the end.

The table on page 882 summarizes 54 cases of cancer of various organs in epileptic patients, showing the average monthly convul-

TABLE SHOWING EFFECT OF CANCER ON FREQUENCY OF CONVULSIONS IN EPILEPTIC PATIENTS. AVERAGE NUMBER OF CONVULSIONS A MONTH FOR A GIVEN NUMBER OF MONTHS PRIOR TO MALIGNANCY IS COMPARED WITH AVERAGE RATE AFTER PROCESS BECAME ACTIVE AND WITH RATE DURING LAST TWO MONTHS OF DISEASE.

	Patient.	Location of cancer.	Monthly convulsion rate before illness.	No. of months counted before cancer.	Monthly convulsion rate during malignancy.	No. of months counted during malignancy.	* Monthly convulsion rate during last 2 months of illness.
1.	J. E. G.	Breast	1	12	0.7	7	1
2.	M. A.	Rectum	5.5	12	0.2	10	0
3.	M. M. C.	Uterus	3.7	12	2.7	9	2.5
4.	J. B.	Face	2.4	29	1.6	29	4.5
5.	S. S.	Hand	4.5	24	1	24	0
6.	E. W.	Axilla	7.2	28	6	28	0.5
7.	J. P.	Mandible	1	6	0.5	8	0
8.	H. B. R.	Rectum	3	12	2	3	2
9.	E. W. H.	Uterus	†				
10.	J. A. B.	Vulva	1.2	12	0.3	3	1
11.	F. P.	Pleura	5.6	12	3.6	12	1
12.	L. E. R.	Stomach	7.5	8	3.5	4	4
*13.	D. D.	Breast	16.2	12	9	10	3
*14.	M. E.	Breast	5.7	3	4.7	3	4.5
*15.	J. M. K.	Breast	0.2	4	0	4	0
*16.	M. J.	Breast	2.2	12	1.3	12	1.5
*17.	B. H.	Breast	6.5	12	4.3	12	3.5
*18.	M. F.	Breast	5.5	12	4.6	12	6
*19.	L. J.	Face	18.9	12	8.1	12	9
*20.	R. L.	Leg	24	12	12	12	14
21.	A. C.	Uterus	0.9	12	2.6	12	1
22.	F. M.	Uterus	10.8	12	10.6	12	8.5
23.	P. B.	Breast	0.8	12	5	12	3
24.	C. M.	Breast	1.5	12	0.9	12	0.5
25.	A. P.	Face	3.7	13	5	13	4.5
26.	E. S.	Uterus	3.2	12	5.5	12	3
27.	A. C.	Breast	1.6	12	1.5	12	0
28.	N. G.	Uterus	6	12	6	12	6
29.	E. W.	Stomach	9.6	12	9.6	13	20
30.	K. G.	Uterus	3	13	6	12	3.5
31.	A. H.	Duodenum	0	24	0	24	0
32.	S. C.	Liver	0.7	24	0.8	6	0
33.	L. H.	Axilla	0.4	12	1	13	1.5
34.	J. T.	Axilla	0	24	0	12	0
35.	J. S.	Liver	0.1	24	0	12	0
36.	S. E. R.	Meninges	1.2	96	0.6	24	?
37.	A. F.	Uterus	4.3	24	3	7	0
38.	A. W.	Brain	8	12	9	6	7
39.	B. C.	Uterus	3	36	2.5	3	2
40.	L. D.	Uterus	10.7	12	2.6	6	2
41.	M. W.	Liver	1	12	0.6	19	0.5
42.	B. F.	Maxilla	?	0	0.1	10	0.1
43.	M. D.	Rectum	?	0	0	6	0
44.	M. F. A.	Testicle-sarcoma	0	12	0	12	0
45.	A. F.	Uterus	5	12	5	8	5.5
46.	H. Y.	Stomach	1.4	36	1.6	9	2.5
47.	K. M.	Colon	0.6	24	0.6	8	0
48.	A. C.	Breast	1.1	48	0.6	32	0
49.	J. S.	Uterus	3.2	24	2.6	3	3
50.	J. H. N.	Duodenum	5	24	6.3	8	14
51.	M. L.	Breast	13	5	16.5	20	9
52.	L. R.	Hand	11.5	6	8.4	5	8
53.	M. K.	Sarcoma of knee	3.7	4	0	2	0
54.	A. I.	Stomach	7	1	2	9	3
		Total averages	4.8	17	3.4	11.3	3.2

* Patient living.
† Convulsion free for 5 years prior to death.

sion rate for a number of months prior to malignant activity, and compares this rate with the rate of convulsions throughout the progress of untreated malignancy and with the monthly convulsion rate during the last two months of the malignancy.

Of the total 55 cases 47 were followed to their termination at death. Only eight of the 55 cases showed an increase in convulsions during the last two months of illness and this might be attributed, at least in part, to the fact that patients who are seriously ill are placed under more constant observation and their convulsions recorded more carefully. Forty-seven cases either were unchanged or showed a decrease in seizures. There was definite decrease in frequency of seizures in 32 of the total 55 cases. In only three cases was the increase in seizures remarkable, while in 22 cases the decrease in seizures was quite marked. Eight patients are still living (No. 13 to No. 20 inclusive), two of whom (Nos. 14 and 15) were successfully operated and treated but no treatment was administered prior to operation, *i. e.,* during the period in which their convulsion rate was tabulated. Case 9 had been free of convulsions for three years prior to the onset of cancer and no convulsions occurred for five years prior to her death although she had been a confirmed epileptic. This case was omitted from the total number used in calculating the total averages. In two cases (Nos. 42 and 43) the convulsion rate prior to the malignancy could not be ascertained. In one case (No. 36) the number of convulsions during the last two months could not be definitely ascertained although the record indicates that she probably had none. The decrease in frequency of seizures, after the malignant process became apparent, is quite consistent in most cases and this decrease in seizures is most noticeable during the last two months of illness. The gradual decrease in convulsions is reflected in the total averages comparing the monthly convulsion rate before the onset of cancer, during the entire period of malignant growth, and during the last two months of malignant growth. Case 13 (D. D.) is still living and is the only one in which we have had opportunity to do clinical laboratory tests. Her CO_2 combining power of blood plasma has ranged between 60 c. c. and 78 c. c. volume per cent since the diagnosis of cancer was made. While in a state of mild alkalosis the frequency of her seizures has gradually declined until now she has been free of convulsions for more than a month.

On account of the limited number of cases reported one avoids conclusions; however, the findings indicate that alkalosis is not entitled to the important position which has been given it in the induction of seizures, or in lowering the convulsion threshold. Rather, one's attention is directed to the favorable influence of dehydration which accompanies chronic diseases and which, in these cases, exerted itself, apparently, in the presence of alkalosis. Obviously, if relative alkalosis in these cases tended to exaggerate their epilepsy, this was more than compensated for in most cases by other physicochemical processes. We may assume that dehydration accompanies such a chronic wasting disease and upon this may depend important physiologic and physicochemical changes, especially increased oxygen tension and colloidal dispersion.[39] The decrease in frequency of seizures is most noticeable during the last two months of illness. During this period hemorrhage from malignant new growth is common and this might have been a factor in the dehydration of some cases.

It has been observed that convulsions tend to decrease in frequency in chronic deteriorated epileptics with generalized flexion rigidity;[40] however, this could not explain the decrease in seizures among our patients who were followed over a relatively brief period of time.

SUMMARY.

The data which have been presented seem to indicate that acidosis and alkalosis are not immediate factors in controlling and precipitating seizures, although they may act indirectly by favoring dehydration and hydration respectively. The influence of oxygen tension on the capillary permeability and the effect of oxygen administration on cerebral functions have been suggested as important factors in controlling convulsions. Attention has been directed to the relation of vasomotor activity to brain metabolism and other, equally obscure, physicochemical processes. In a review of 55 cases of malignancy complicating epilepsy it was shown that the number of seizures decreased as the malignancy progressed. Only eight of the 55 cases showed an increase in seizures during the progress of the malignancy. There was either no change or a decrease in seizures in 47 cases. There was a definite decrease in frequency of

seizures in 32 of the total 55 cases. Alkalosis, which may be associated with cancer, obviously does not induce seizures in epileptic patients. Cachexia and dehydration incident to malignant neoplasms probably raise the convulsion threshold which accounts for the decrease in seizures.

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DISCUSSION.

DR. TEMPLE FAY (Philadelphia, Pa.).—*Mr. Chairman and Members of the Section:* I believe this is one of the most important papers that has been presented in the past few years and out of the maze of material that has come to light, it shows clear thinking and direction of purpose which is all important if we are to reach a solution of this convulsive problem.

In the first place, Dr. Hodskins has brought to your attention the importance of emaciating diseases. Four years ago we were struck with the fact that in diabetes and in tuberculosis and in malignancy, representing a large group normally of our population, convulsive seizures do not begin or progress in those groups unless there is direct metastasis to the brain. Dr. Landis, of Philadelphia, and Dr. Morgan, who are active specialists in tuberculosis, have told me that it is very unusual to see epilepsy developing in a well-established case of tuberculosis, although tuberculosis may develop in the epileptic.

Dr. Timme of New York and Dr. Petty of Philadelphia, both interested in diabetes as a specialty, have told me of similar experiences throughout a lifetime. It is rare to find epilepsy developing in or convulsions developing in the well-established case of diabetes until insulin is given, and then usually a hydration state follows with the better metabolism of carbohydrates.

In the third group, those that have to do with malignancy, Dr. Pancoast in the roentgenographic work at the University of Pennsylvania and Dr. Chamberlain at Temple University, with a great deal of experience, have said again without brain metastasis it is extremely rare to see convulsive seizures or epilepsy beginning in the malignant groups.

Here nature has divided those emaciating conditions on the one hand and freed them of convulsions as Dr. Hodskins has pointed out. On the other

hand in the fat, hydrated hypopituitary types, we find the seizures commonly occurring not only in the epileptic but throughout the various incidences of the convulsive states. Here is, therefore, a line of approach already indicated in the broad distinction between the dehydrated and the hydrated groups—Whether it be dehydration alone is a matter to be determined. But I would say here what my feeling regarding dehydration is, as I have stated it in three articles already published, I do not believe the fluid itself nor the pressure which it produces has anything to do with the precipitation of the attack. I do believe that the fluid does predispose the individual to the attack and it predisposes the individual, in my opinion, by actually displacing an appreciable amount of blood volume and consequently oxygen from the cranial vertebral cavity whose limits are fixed at the moment. Thus we have a relatively low-grade anoxemia produced which may be periodic, preparing the patient for an extraordinary response to a vascular or sympathetic disturbance that in the presence of an appropriate sensory stimulus and defective inhibition may precipitate the attack. That is as far as I believe dehydration can assist in the problem. It does improve cerebral circulation, and the improvement in cerebral circulation is because after subtraction of the fluid volume by dehydration there is more opportunity for blood within the cranial cavity, better oxygen utilization and therefore a better tone of inhibitory control so that sensory impulses which fundamentally upset this mechanism and produce a convulsion are better controlled and the motor centers do not spontaneously respond as they do under conditions of partial anoxemia.

We must get two things clearly in mind if we are to arrive at any solution of this problem. The first is that a convulsion, if it is a major seizure and characterized by violent clonic manifestations, indicates that the motor cortex is functioning and not only functioning but violently functioning, or the subcortical distribution of motor influences are actually functioning throughout the period of attack. It is impossible to obtain hyperfunction out of a diseased motor cell. You have Jackson's law to that effect.

It is also impossible to maintain motor function or any cortical cellular function without an adequate oxygen supply throughout the entire period of function. Therefore, anoxemia alone cannot be the factor, neither can it be a complete anoxemia, because we would have a complete loss of function as we see in a cerebral arterial thrombosis; where there is no oxygen available to the brain cell, there is no function. Therefore, we must predicate only a selective and partial anoxemia.

We have several clinical examples of this, Stokes-Adams' disease for instance. It has been shown when the heart skips a certain number of beats, convulsive seizures are likely to occur. On the other hand with a temporary profound oxygen lack we see what is usually called syncope. On the operating table when the patient's blood pressure suddenly falls to zero; the cortex becomes gray-white and pulseless but the individual does not go into a convulsive seizure. Cobb believes, as he stated in the last (May 1932) Archives of Neurology and Psychiatry that if cerebral anemia occurred suddenly, every individual dying a natural death would have a convulsive seizure. I

do not believe our records in the hospital or in the war show that the individuals who died suddenly, were shot or executed, all manifested terminal convulsive seizures. Certainly the patients in my experience who have died suddenly on the operating table or died suddenly in the wards with brain tumors or died of cardiac failure or respiratory failure, have not had terminal convulsions. The incidence of a terminal convulsion is as rare in cases of sudden death as it is in the population at large and as stated above it requires the continuation of oxygen supply to some degree, not its total subtraction to maintain a convulsive seizure.

We must not place too much emphasis on the theory of acid base relationships, neither should we on the oxygen basis or the hydration basis, but upon the efficiency of cerebral circulation, however that factor may be influenced. To contend, as many have contended, that one factor or the other is the more important, is only to confuse the issue. We have a combination or interrelation of all factors. If we are to attack the problem from the standpoint of actual function in the motor area we must admit that between attacks it is normal and no constant pathology has ever been demonstrated. Not until late in the picture does true motor weakness appear. A major generalized convulsion may be compared to a runner or the individual who is doing violent physical exercise, though the movements are purposeless there is no weakness until exhaustion ensues. I believe we shall find the origin of these "normal" uncontrolled movements due to a defect in the sensory mechanism as responsible for the impulse and for the radiation of that impulse as well, and we are going to pay less attention to the actual *post hoc, ergo propter hoc* ideas of seeking to visualize a pathology of the motor cortex involving all of these cases. Certainly I have seen and I know every one here has seen few examples out of hundreds of cases that could be actually ascribed to demonstrable organic pathology of the motor cortex.

I believe Dr. Hodskins has raised three important considerations. In the first place, the acid base equilibrium is not the determining factor. In the second place, we have been able to maintain patients on dehydration without the advent of acidosis. Thirdly, the results obtained have been proportionate to our ability to balance body fluids and improve cerebral circulation. In approximately 65 per cent of the cases, in my series there has been definite mental and seizure improvement. Only 11 per cent has been attack-free for a five-year period; 23 per cent has totally failed to respond to any method or combination of methods, including the use of phenobarbital, that we have been able to devise. There are frequently abnormal mechanisms that disturb cerebral circulation that are insurmountable, such as jugular foraminal stenosis, developmental defects and organic pathology.

I believe now the attack on the problem both physiologically and clinically is becoming directed toward a mechanism, a symptom complex, which may be influenced by the volume of blood actually circulating within the brain with the recognition that this volume of blood may easily be displaced and decreased during periods of hydration because of the increase in the volume of interstitial and spinal fluid. Under conditions of dehydration this blood volume may be increased and permit a better cerebral circulation. In the

end, it amounts to better oxygenation. I do not feel that we accept profound anoxemia alone as the factor responsible for the attack because there must be sufficient oxygen present to keep the motor cells functioning for a period of three to five minutes, or perhaps five hours if we have a case of status epileptics, and certainly there is enough oxygen entering and CO_2 leaving that field to permit those motor cells to go on functioning, as they do, uncontrolled.

Dr. Alfred Gordon (Philadelphia, Pa.).—We are very fortunate indeed to have Dr. Fay with us in conjunction with Dr. Hodskins. The problem of dehydration is certainly a very interesting and important one to anyone who is interested in the therapeutic side of epilepsy, the disease with which every one of us has so much trouble.

When Dr. Fay first came out with his suggestion concerning dehydration, without question I immediately attempted to keep records of my cases with dehydration according to his method, according to his system and according to his views. I may say to Dr. Fay, as well as to Dr. Hodskins, I have a few cases with dehydration who were improved, but I also have a mass of cases that have not improved.

The proper stand for us to take is to try to test everything that a man of standing advances. This is my experience. If I am not mistaken, Dr. Fay originally based his ideas of improvement by dehydration on the fact that with this process, there was diminution of intracranial pressure. But is it so? I refer you to the works of equally competent men, Dr. Fremont-Smith particularly, who from clinical experimentation arrive at the conclusion that during dehydration, the diminution of epileptic seizure is not due to the diminution of intracranial pressure. Dr. F.-Smith published several articles of this kind. He also proved it experimentally corroborating it by clinical observations that the diminution of intracranial pressure is not the result of diminution of water in the system. In view of Dr. Fay's observations he is also puzzled. There is therefore no definite conclusion with regard to the increase or decrease of intracranial pressure as a factor in epileptic seizure.

I believe that Dr. Fay today showed considerable conservatism with regard to his original ideas and original thoughts. I was delighted to hear it. In medicine it is difficult to make mathematically correct and exact statements because there are so many factors which enter into the causation of certain disorders.

With regard to the anoxemia, I would ask a question of Dr. Hodskins and Dr. Fay.—If I am not mistaken, both of these gentlemen place considerable weight on the anoxemia. In the cases of carbon monoxide poisoning, the entire picture, at least the physical manifestations, is the result of anoxemia. There is no chemical element that enters into closer combination than carbon monoxide with blood; it replaces the oxygen, and we have a deep anoxemia. I have seen a number of cases of carbon monoxide poisoning and I did not observe any convulsions, consequently, I do not believe that anoxemia, which these two gentlemen stressed and dwelled upon, could

account for the convulsive seizures because anoxemia is the most striking phenomenon in carbon monoxide poisoning. I would like to ask both Dr. Hodskins and Dr. Fay whether they will modify their opinion or not dwell so much on the element of anoxemia in the production of convulsive seizures.

DR. TEMPLE FAY (Philadelphia, Pa.).—*Mr. Chairman and Members of the Section:* In the first place, this was not to be a wet and dry issue this morning and I think that Dr. Gordon has inadvertently raised the issue which we had hoped perhaps wouldn't be raised. But since he has raised it, let me say this in explanation of the apparent discrepancy that he has mentioned, that in analyzing the group of so-called dehydrated patients it was found that the seven patients which Fremont-Smith, Merritt and Lennox placed on a dehydration program failed to lose any body weight, even though the intake of liquid was limited to 500 c. c. for five days. These patients actually produced from 1000 to 1360 c. c. of urine beside what they lost by skin, breath and bowels, and one case gained three pounds in weight besides. In other words, they voted dry and were wringing wet.

This is not dehydration as I have seen it. If you do not subtract tissue weight from the body, you do not get dehydration. Dehydration means withdrawal of fluid not from the diet but from the body.

Dr. Gordon makes reference to his cases. I have had several cases that have come through the various clinics here, and in which diet was not controlled and the individual was left either to misrepresent his reports or to get adequate fluid from other sources than those which were intended.

If the members of the Association desire to see five patients now on dehydration at Temple University Hospital, with a fall in pressure and with a consequent fall in spinal fluid volume which has been measured during the past week and were prepared for the paper which was to be presented here this morning, I will invite them to come out and make the pressure determinations and see dehydration as it should be done. Therefore, I am inclined to object to Dr. Gordon's remarks on the basis that his cases were probably not controlled by diet and if they did show a progressive loss of weight, they were dehydrated; if they did not, they certainly were not dehydrated, although you cut down the volume of fluid they actually consumed by glass or told them not to drink so much water.

I believe that my position here is anomalous. I shouldn't have the right to rediscuss any factor, but I do think it is important to correct what has been placed on the program and what Dr. Gordon has already stated, that in my earlier work I felt that increased intracranial pressure was the cause of the attack. Unfortunately, the members who have taken that reference have confused two issues. I feel that increased intracranial pressure is the cause of the atrophy of the brain, but in no reference in any paper have I made the statement that is attributed to me here. I know of hundreds of cases of increased pressure without attacks. It is obvious that increased intracranial pressure is not the cause of an attack. Furthermore, if Dr. Gordon will read the literature, he will find I have made that statement three years ago in my first article that was published. So that I believe there is no issue

before the house on the wet and dry question. I think we shall all agree when we get all the facts together, but, just as Dr. Wortis has said, too much emphasis has been placed on special programs and we haven't all of our facts as yet. I apologize, Dr. Hodskins, for having taken this time.

Dr. S. Bernard Wortis (New York City).—I believe our difficulty, at this moment, is that we are all trying to develop one mechanism for the cause of convulsions. Brain hydration acts in many instances as the cause of convulsions; in many instances tumor is the cause. Recently Cobb has been able to definitely define 13 physiological mechanisms causing convulsions, and of these 13, anoxemia forms one group which is rather large. Brain scarring with shunting of impulses forms another large group; and then there are several other groups of convulsions caused by various drugs, viz., insulin, camphor, absinthe, cocaine, etc., for which we at this time do not know the mechanism. It seems we are a bit premature in attempting to formulate a common mechanism for all convulsive seizures.

I want to thank Dr. Hodskins most cordially for his very valuable study. This type of work, to my knowledge, has not been done before. It represents a most valuable statistical study and helps to direct experimental laboratory work.

His observation that caffein sodium benzoate in very large doses diminished the number of convulsive seizures is most interesting. Similar results were reported by Keger and Perritz a number of years ago.

I would like to add another observation which I think may have been forgotten; that is, if one measures the manometric spinal fluid pressure following caffein sodium benzoate injection, there occurs simultaneously a marked reduction of the manometric pressure of approximately 15 to 30 millimeters (of spinal fluid—Strauss manometer used) which persists in part for approximately 30 minutes. These observations were made and reported to the Association for Research in Nervous and Mental Diseases (1927) by Dr. Stevenson, Dr. Christensen and myself several years ago and were confirmed by Dr. Denker (Am. J. Med. Sciences 1929).

Dr. Alfred Gordon (Philadelphia, Pa.).—There is just one more question, if you don't mind. I would like to ask Dr. Fay and Dr. Hodskins in their conclusions to tell us whether in addition to the material element in the production of epilepsy, they have ever considered the pyschological level of convulsive seizures.

Dr. Morgan B. Hodskins (Palmer, Mass.) (in closing).—I tried to make it plain in the paper that this wasn't an attempt to explain epilepsy at all, that wasn't our idea. It simply was an attempt to put on record a certain number of observations of the way epileptic people responded to different conditions.

Dr. Gordon asked a question about the psychogenic factors in epilepsy. I have considered those and to be perfectly frank with you, the more I consider them, the more confused I am about just what it all means.

MENTAL DETERIORATION AND DEFICIENCY.

Its Consideration from the Standpoint of Certain Cererbral Vascular Volume Relationships.*

By DR. TEMPLE FAY, Philadelphia.

PART I.

Mental deficiency is a relative behavior and intellectual disturbance which cannot be subjected to analysis by animal experimentation.

The institutionalized mentally deteriorated human beings have been committed after the deterioration is evident, and offer little opportunity for consideration of the processes responsible for the mental change. Many cases that deteriorate while in institutions undergo such slow involutional retrogression that these are not subject to striking changes associated with any recognizable process.

In the hope of throwing further light upon this important problem, certain cases which have demonstrated rapid mental deteriorating changes while under observation for acute neurosurgical conditions, are presented, as the analogy is justifiable. The chief difference lies in the period of time involved and the chronicity of the process.

Individuals who demonstrate an acute loss of mental activity and develop marked signs of mental deterioration, within one to six weeks, and who respond to certain treatments after temporary adjustment is attempted, form an interesting problem for study. These cases frequently find their way eventually into the institutionalized groups, or become chronic, deteriorated patients under active supervision after such acute episodes.

Cases have been observed on the neurological service that became rapidly dull, apathetic, slow in speech, with marked delay in their responses to questions, demonstrating also difficulty in memory retention and the performance of complicated commands, with marked decrease in their psychomotor activity and showing the characteristic reactions of a profoundly deteriorated patient.

*Read at the eighty-eighth annual meeting of The American Psychiatric Association, Section on Convulsive Disorders, Philadelphia, Pa., May 30, 1932.

This is characteristic of patients who have demonstrable tumors of the third ventricle, the fourth ventricle, or cerebellar tumors which produced acute internal hydrocephalus by obstruction of the spinal fluid outlets, so that there is an over-accumulation of spinal fluid and consequent internal hydrocephalus. The acute phases of this type of internal hydrocephalus may be established within one to two days, and the individual pass from an apparently normal state into the distinctly dull, apathetic conditions described above.

If ventricular puncture is undertaken and the fluid released, there follows a prompt and immediate return of mental activity, and the patient appears normal again within 24 to 36 hours. If these acute cycles are repeated and ventricular drainage instituted to correct the pressure, the same phenomena may be observed; but if the hydrocephalus is not correctable, as is sometimes the case, even with removal of the tumor masses, the individual gradually deteriorates and with the subsequent release of the ventricular fluid under pressure, there is a lessened tendency to return to the former normal mental activity; and this is associated by demonstrable increases in the size of the ventricles, with the obvious loss of cortical volume, as the internal hydrocephalus advances.

During the past five years an attempt has been made to arrest this type of mental deterioration, or correct the acute phase in its early stage, so as to prevent the disastrous mental sequelæ which are usually encountered and well recognized in organic pathological states.

Group I.

BRAIN TUMORS ASSOCIATED WITH ACUTE PRESSURE PHASES.

Tumors of the third ventricle and cerebellum, or posterior fossa tumors which compress the aqueduct give rise to an acute internal hydrocephalus, in many instances. The patient passes rapidly from a normal mental state to one of dulness, apathy, retardation of psychomotor activity, and obvious deterioration, often repeatedly and rapidly advancing into stupor. The marked relief of these symptoms occasioned by ventricular tap and release of intracranial pressure, and by withdrawal of ventricular fluid, is well known, and a striking return to practically a normal state of mental acuity follows within 24 to 48 hours. When removal of the tumor or

obstruction is possible a permanent relief of these pressure symptoms has been afforded. In cases where the tumor is inoperable or has produced an obstruction which cannot be relieved, repeated ventricular drainage has been necessitated, and with each acute cycle of intracranial pressure there have been induced mental obtundity and loss of acuity noted above.

As the hydrocephalus increases and there is an evident loss of cortical volume by compression, the recovery from these repeated cycles of pressure is less apparent and the patient gradually becomes mentally deteriorated, and eventually succumbs. Of the many cases that could be presented to illustrate these striking reactions, the following will serve as a typical example, illustrating the cycles which may be encountered in obstructive hydrocephalus, due to a pineal tumor extending into the third ventricle.

CASE I.—Miss H. J., white, single, age 20. Referred by Dr. J. A. Brooke. Admitted to Temple University Hospital, service of Dr. Temple Fay, on November 28, 1931.

Chief Complaint.—Failing vision, diplopia, mental torpor, headache and vomiting.

History of Present Illness.—Was well until June, 1931, excepting for otitis media on right with chronic drainage over a period of 12 to 14 years. Drainage stopped in April of 1931. A few months later patient complained of headaches with morning vomiting. Eyes examined and gastro-intestinal studies were made without relief. Three months later, ataxia, headache, vomiting and diplopia became pronounced and vision began to fail.

On admission to Temple University Hospital, patient showed a bilateral sixth nerve paralysis, choked disk of five diopters, marked ataxia and cerebellar incoordination with dysmetria on the right, facial weakness on the right, hypesthesia in the right trigeminal distribution, deviation of the tongue to the right, moderate deafness on the right, tenderness to deep pressure over the right mastoid, and hypotonia with loss of all deep tendon reflexes.

Wassermann was negative. X-ray of the mastoids showed a chronic suppuration in the right petron. Barany examination indicated a mass lesion in the right cerebellar hemisphere.

Diagnosis: Right cerebellar abscess.

A radical mastoidectomy on November 30, 1931, by Dr. Matthew S. Ersner revealed no extradural pus. Operation immediately followed by right suboccipital cerebellar decompression (Dr. Temple Fay) with exploration. No abscess was encountered in the cerebellar hemisphere. Ventricular puncture with release of fluid under extreme pressure. Exploration revealed a pineal tumor extending into the third ventricle. A portion of the tumor was removed.

Diagnosis: Pinealoma extending into third ventricle. Ventricular canula was permitted to remain in right ventricle for 36 hours, affording continuous ventricular drainage.

After the post-operative period, the patient showed marked improvement with return of mental activity and by the fourth day was free from diplopia; facial weakness had cleared, and patient responded normally to questions and conversational activities.

Five days after operation the patient became dull, drowsy, partially irrational, vomited, but complained of no headache. Dehydration by magnesium sulphate and fluid limitation resulted in improvement so that the patient was again clear and mentally active on the eighth day. Marked improvement occurred coincident with a spontaneous cerebrospinal leak which required secondary closure. With cessation of spinal fluid drainage, the patient again became quiet, dull, unresponsive, vomited occasionally, and showed signs of intracranial pressure in spite of cerebellar decompression. The wound was under tension.

A reexploration on December 30, 1931, with second attempt to remove remaining portion of tumor in the third ventricle was performed. Further tumor tissue was removed with tentorial decompression by incision of the incisura and section of the tentorium to the margins of the lateral sinus. Ventricular drainage at this time revealed fluid under 16 mm. Hg. pressure. Approximately 2 ounces were obtained. The flow then stopped. Intravenous saline infusion given on the table and about one ounce more of ventricular fluid began to flow from the canula within five minutes, after the beginning of the infusion. Patient returned to her former mental activity, received guests, was bright, alert, happy and optimistic.

Ventricular tap February 3, 1932, because patient began to vomit; showed progressive intracranial pressure signs with mental dullness and marked apathy, incontinence and definite signs of deterioration (Fig. 1). Drainage of two and one-half ounces of ventricular fluid under 16 mm. Hg. and blood transfusion. Patient showed gradual improvement during the next two days. Pulse fell; diastolic pressure improved, urinary output increased and voluntary control of urine followed the next day. Forty-eight hours later, patient was alert, responsive, comfortable and showed no signs of pressure, but showed definite evidence of mental deterioration. Her conversation was less spontaneous. Replies were correct but brief. She would smile and respond but remained apathetic, although carrying on all other mental processes in a normal way.

Intracranial pressure signs recurred requiring ventricular drainage on February 21, 1932. There developed severe frontal headaches, vomiting, signs of intracranial pressure associated with semi-stupor. Output showed marked diminution associated with gain in body weight. Ventricular drainage was followed by marked improvement. Patient rapidly returned to almost the former mental state. She received friends again and was permitted to sit up in bed. A sudden attack of acute intracranial pressure on March 7, 1932, caused patient to become dull, confused, difficult to arouse and ventricular

puncture with removal of 2 ounces of fluid under 18 mm. Hg. pressure was performed. Bulging of the decompression receded. Following this, the patient never regained mental acuity but remained dull, listless and definitely deteriorated. She was discharged on March 13, 1932, after another ventricular drainage, in a dull, deteriorated state under the care of a nurse in her home.

The patient improved at home and for three weeks made rapid progress although mental activity was definitely retarded and responses were childish and simple. Another ventricular drainage was required. Three ounces of fluid were removed under 12 mm. Hg. pressure in the patient's home.

Following this, patient improved to a point where she was allowed to sit up in bed, but her mentality had become profoundly deteriorated and further measures of relief were abandoned by mutual consent of the family and consulting physicians. The remaining days were spent in a dull, apathetic state, incontinent and requiring constant nursing and feeding. Patient died April 18, 1932.

Group II.

Acute communicating types of hydrocephalus due to inflammatory obstruction of the basal cisternæ or Sylvian sulcus.

Certain cases which have survived attacks of acute meningococcic meningitis, cases of posttraumatic and spontaneous subarachnoid hemorrhage with adhesions, and idiopathic infantile types; probably unrecognized tubercular meningitis or failure of the Sylvian sulcus to transmit spinal fluid to the cortex, form the basis for these observations.

The phenomena are illustrated in Figs. 2 and 3 (Case II) by encephalography where a communicating type of hydrocephalus is present, and the obstruction definitely shown in the Sylvian sulcus just lateral to the cisterna chiasmatis. Here increased intracranial pressure was present with enlargement of the basal cisternæ, and definite secondary internal hydrocephalus, due to back-pressure and inability of the fluid to escape through its normal outlets, even though the ventricular system was opened and drainable by the lumbar route permitting an air injection.

Case II.—Baby R. Y., white, male. Age ten months.

Admitted to Temple University Hospital, Service of Dr. Temple Fay, on November 9, 1931, with history that at age five months the mother noted that the child was having spasms during which his eyes rolled upward, arms stretched outward and legs were drawn up. Attacks gradually intensified until eyes twitched, mouth quivered, became intensely flushed over entire body,

and gave a shrill cry. Extremities became spastic and back arched. Attacks occurred from 10 to 30 times daily.

July, 1931, diagnosed Schilder's Disease by Dr. William G. Spiller.

Past history revealed that the child was a full term, normally delivered male weighing seven pounds. No labor difficulty. Apparently perfectly normal until onset of present condition. No feeding difficulties. Gained weight rapidly. Had first tooth at age eight months. Could support head until onset of illness and mother stated that hearing began to diminish at age six months.

Examination showed a well-developed, well-nourished male baby of ten months. Moved all extremities readily. Could not hold head up. Question whether child could see or hear.

On November 10, encephalograms were taken. Initial spinal tap under local anesthesia with patient in horizontal position was 10 mm. Hg. and when patient was carefully turned to sitting position pressure rose to 30 mm. Hg. 87 c. c. cerebrospinal fluid was permitted to drain off and 70 c. c. of air introduced into canal and then patient sent to X-ray for films. The films showed a complete sealing off of the subarachnoid spaces over the cerebral surfaces. Air made its way readily to the ventricles and the basal cisternæ. There was no air at all in the usual subarachnoid spaces over the convex surfaces of the brain. The ventricular system and all of the basal cisternæ were definitely enlarged.

Diagnosis: Communicating hydrocephalus. Obstruction of the Sylvian sulcus in the region of the operculum.

Following the encephalogram, the temperature and pulse rose but gradually returned to normal. The child seemed to see objects held at close range and to hear, since he looked at examiner and smiled when spoken to in an ordinary tone. Condition good.

On November 12, 1931, an exploratory craniotomy was performed in the left parietal area. Marked subarachnoid edema of brain noted. Plastic arachnoiditis in Sylvian area. Arachnoid fluid spaces opened and drained through dura to scalp. Rubber dam drainage for 48 hours.

Temperature rose to 107, post-operative, by rectum. Cold packs and sponging were resorted to.

Three days after operation, temperature fell and condition improved. Had Jacksonian movements in both upper extremities at times.

Two days later less movements of extremities noted, especially on the left. The child improved rapidly and seizures became infrequent. Child discharged in improved condition and has continued to improve to the present time. Seizures have ceased. Child ten months after operation attempting to crawl, talk and play with toys. Shows distinct mental retardation but no signs of former stupor. Total intake of fluids has been strictly curtailed to 16 ounces daily. Growth apparently normal.

The clinical course in these cases represents that of an acute internal hydrocephalus, with rapid mental deterioration, and in Case III (A. V.) led to the diagnosis of cerebellar tumor, due to the huge

dilatation of the ventricles and certain cerebellar signs associated with headache, choked disk, vomiting and mental deterioration, terminating in stupor. Emergency spinal drainage (dangerous) relieved the symptoms in this case temporarily. There was an immediate return of mental acuity without signs of deterioration. Repeated ventricular punctures relieved the periodic attacks of stupor. An exploratory operation of the cerebellum revealed no tumor. The final mental deterioration was followed by autopsy which indicated an inflammatory lesion in the Sylvian sulcus, post-hemorrhagic in origin. (Figs. 4 and 5.)

CASE III.—A. V., Jr., white, American, male, age nine.

Referred by Dr. Frederick Leavitt.

Admitted to Temple University Hospital, service of Dr. Temple Fay, on October 1, 1929, after the following series of events:

June 20, 1929, became dizzy after unusual excitement and was put to bed. Later was found unconscious on the pavement outside his bedroom window from which he had apparently jumped. He remained unconscious for 20 hours. Received severe injury over right eye. He soon became apparently normal.

Several weeks later he started to complain of severe frontal headaches and occasional pain in the dorsal region of the back. Then had paraesthesia (pins and needles sensation) in right thigh.

An appendectomy was performed July 19, 1929. Had an uneventful recovery.

After his return home, paresthesia, severe headaches and pains in spine recurred. Right upper arm felt numb.

August, 1929, had generalized convulsion with tonic contraction in all extremities. Not fully conscious following this; drowsy, manifested no interest; rolled tongue from side to side and bit it.

August 27, 1929, was admitted to the Orthopedic Hospital. A Queckenstedt test was performed followed by collapse, and four emergency ventricular punctures were required for relief of pressure and respiratory embarrassment.

The patient showed definite cerebellar signs; ataxia, high choked disk and internal hydrocephalus. Ventriculogram showed intense internal hydrocephalus with dilatation of the lateral and third ventricles.

Diagnosis: Cerebellar tumor.

The patient was transferred to the Jewish Hospital, service of Dr. Temple Fay on September 18, 1929, for suboccipital craniotomy. Exploration revealed dilated cisterna magna with signs of thickening of the arachnoid. No tumor revealed.

The patient recovered from stupor after a stormy post-operative period requiring repeated spinal fluid drainage.

Five days after operation, it was noted that the patient was totally blind, though general condition seemed improved.

On September 26, condition again became critical and ventricular puncture again performed. Much fluid was removed.

On October 1, 1929, transferred to Temple University Hospital. On admission it was found that the thighs and legs were emaciated; feet were cold and there was tremor of hands. Reflexes were not elicited. His general condition, however, was improved.

Two days after admission, mental acuity good. Answered and understood questions rationally.

On October 6, an increased amount of spasticity of the extremities was noted. No pathological reflexes could be elicited.

October 8, patient was well oriented. Sensation was normal.

On the eleventh of October, a sudden change was noted in his condition. Temperature rose to 103; pulse 172 weak and irregular; respirations shallow; blood pressure 130/94.

Callosal puncture performed with drainage of ventricular fluid.

Three days later, October 14, 1929, patient died.

Neuropathological findings: Low-grade pial fibrosis at base of brain—Intense around cisterna chiasmatis and Sylvian fissure.

Case II (R. Y.) had been diagnosed Schilder's disease. The child was seen at eight months of age and was found to be dull, apathetic, and apparently blind and deaf. It had been semi-stuporous for two months and had numerous convulsive seizures. Encephalogram (Figs. 2 and 3) revealed an internal hydrocephalus, an increase in intracranial pressure and obstruction in the Sylvian sulcus and cisterna chiasmatis. Exploratory craniotomy revealed intense subarachnoid edema. Direct cortical drainage to the subcutaneous areas and proper fluid elimination and balance were followed by a return to consciousness and activity, and proper fluid balance during the ensuing nine months has led to slow but definite mental proggress so that the child now at 14 months of age has been free from convulsive attacks, is attempting to walk, says a few words, sees and understands to a limited degree; plays with toys, and although definitely retarded and deteriorated has shown marked progress considering the semi-stuporous state in which it existed for two months prior to spinal fluid drainage, encephalogram and dehydration.

Case IV (B. L.) represents the terminal state in an obstructive hydrocephalus (internal and communicating) following a proved meningococcic meningitis, where repeated cycles of mental deficiency were followed by periodic improvement, when excessive cerebrospinal fluid was removed. The final rapid mental deterioration followed uncontrollable increased intracranial pressure.

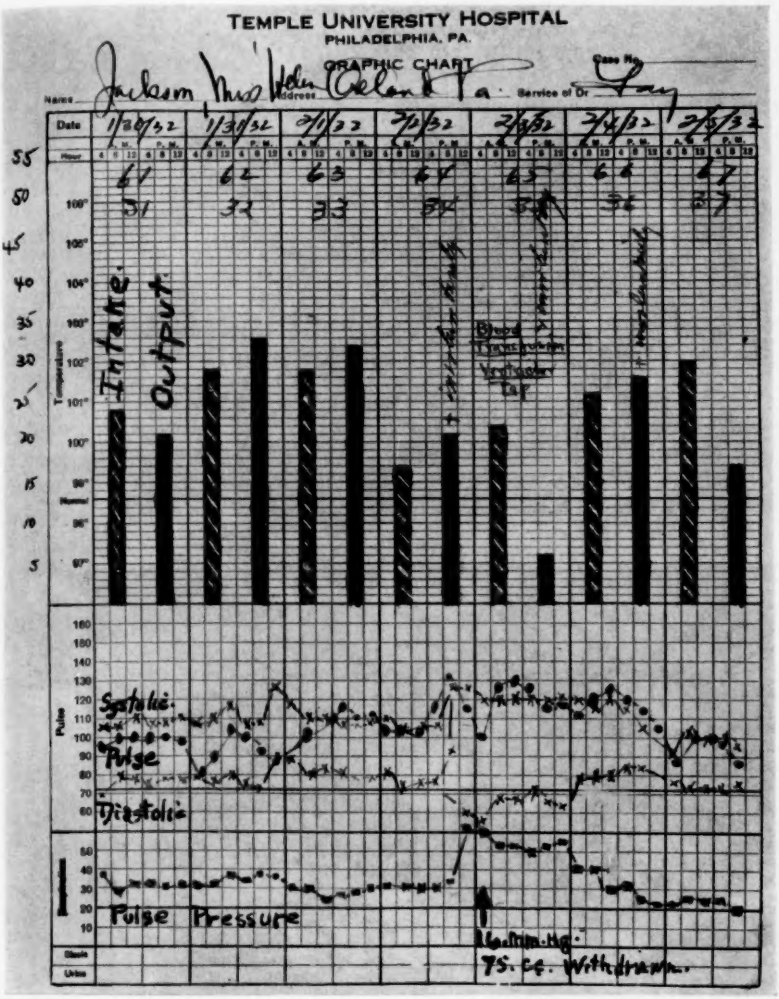

FIG. 1.—(Case I. H. J.) Hospital record showing acute phase of intracranial pressure with abrupt rise in pulse pressure and fall in diastolic pressure. Note fall in pulse just prior to ventricular tap. Incontinence during the three days of mental obtundity. Improvement after withdrawal of 2½ ounces (75 c. c.) under 16 mm. Hg. pressure. Note fluid limitation to 30 ounces. (900 c. c.) with intake and output record, systolic, diastolic and pulse pressure readings.

FIGS. 2 AND 3.—(Case II. R. V.) Lateral encephalogram showing air which was introduced into the lumbar sac has reached the ventricles and the basal cisternæ but all efforts to obtain further progress to the cortex failed to open the usual pathways in the region of the operculum.

Diagnosis: Obstructive arachnoiditis in the Sylvian sulcus.

Note the type of communicating hydrocephalus showing dilatation of the cisterna chiasmatis, cisterna pontis, cisterna magna, IVth ventricle, aqueduct and IIIrd ventricle with definite degree of dilatation of the lateral ventricles.

Fig. 3 (Case II. R. V.) Lateral encephalographic spinal drainage; direct cortical drainage and dehydration with fluid balance. Subsequent 10 months followed by gradual mental improvement.

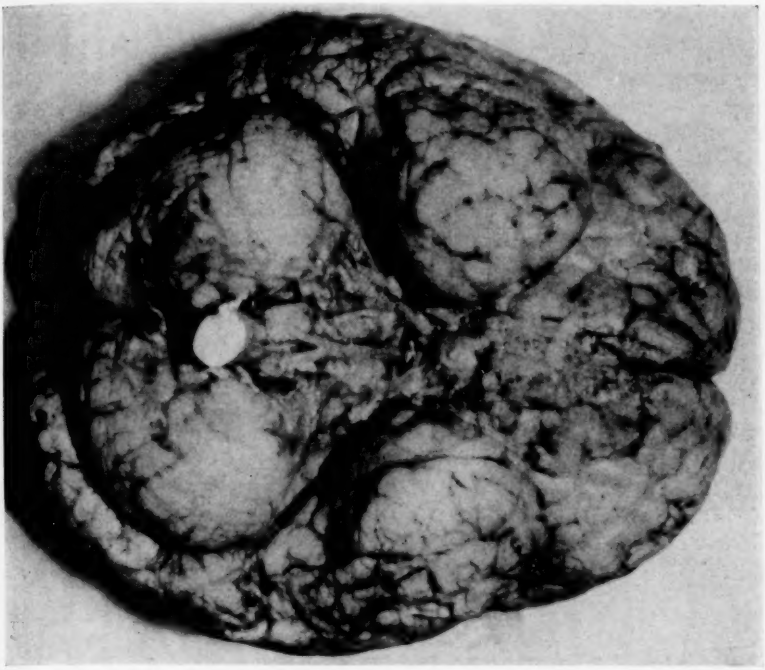

FIG. 4.—(Case III. A. V.) Base of the brain with marked thickening of the arachnoid in the region of the cisterna chiasmatis and at the base of the frontal lobes. The arachnoid has been opened and on one side shows its firm structure and the deep dilated cisternal cavity. No fluid pathways noted over the convex surface of the brain. Adhesive arachnoiditis in the Sylvian sulcus. Pial fibrosis marked in this area considered secondary to post-traumatic subarachnoid hemorrhage.

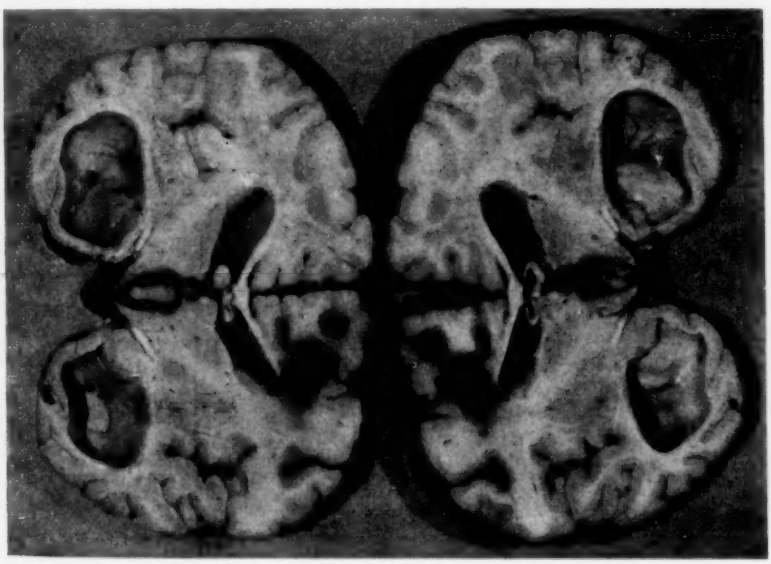

FIG. 5.—(Case III. A. V.) Coronal section of the brain showing marked dilatation of the posterior horns of the lateral ventricles and of the cavities (definitely compressed by poor specimen fixation). Recent hemorrhage in the parietal area secondary to terminal ventricular puncture.

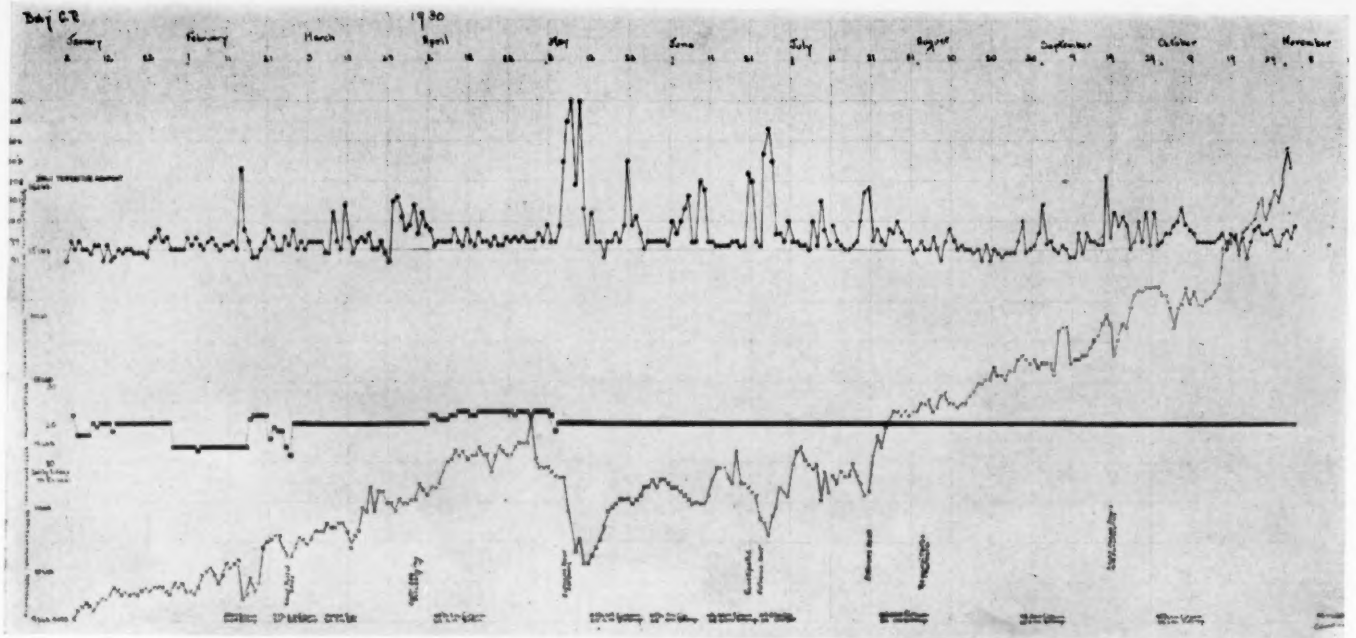

FIG. 6.—(Case 5. C. P.) Chart showing ten months of observation on temperature and weight relations in regard to fixed fluid intake in a potentially hydrocephalic baby where dehydration has been maintained during the past two and one-half years. Note gradual increase in body weight in spite of limitation of total fluids to sixteen to twenty ounces per day during the first five months. Note marked rise in temperature and coincident fall in body weight during intensely hot days encountered in May, June and July.

Bitemporal measurement decreased 8 cm. between February and March. Circumferential measurement showed 2 cm. increase in 10 months. Final weight within 3 pounds of normal age weight. Showed progressive normal development of mental faculties and is, at the present time, normal in speech and activity excepting for disturbance of motor function occasioned by the meningocele.

CASE IV.—B. L. Age five. Admitted to Jewish Hospital, April 5, 1932, to the service of Dr. Arthur Dannenberg, with proved meningococcic meningitis.

Responded to intravenous and spinal therapy. Improved for two weeks, but with recurrence of symptoms and reestablishment of treatment associated with acute phases of intracranial pressure. Daily spinal drainage, marked mental torpor and hebetude during periods of pressure, relieved by spinal drainage. Progressive signs of acute internal hydrocephalus. Encephalogram performed by the cisternal route, ventricles drained, and air introduced. This showed no obstruction to the outlets of the ventricular system but marked obstruction in the region of the cisterna pontis and cisterna chiasmatis. Repeated cisternal punctures with drainage required to correct symptoms of headache, vomiting and stupor.

Patient now deaf, blind, unresponsive and with almost total mental deterioration.

Fluids are not limited, because of the acute infection. The patient has been subjected to spinal drainage when over-accumulation of spinal fluid has occurred.

Patient continues in a state of apathy; blind, deaf, responds poorly to stimuli, and makes no attempt to talk or make his desires known.

Case V (C. P.) indicates the care required in the balance of body fluids during a 10-month period, so as to control the progressive hydrocephalus which was well established at the beginning of treatment. The difficulties in combatting sudden rises in body temperature at times are indicated in the chart (Fig. 6) and rapid loss in body weight represents excessive evaporation during period of hot weather. In this case constant sponging was resorted to rather than permit an increase in fluid intake, although it is evident that fluid could be increased to a point that would permit a stationary weight and thus assist in the body needs for fluid under these conditions. That the head decreased 8 cm. in the bitemporal measurements and the circumference increased only 1½ cm. during the ensuing months indicates the degree of control obtained by placing the total fluid intake at not more than 20 ounces for 24 hours, inclusive of food and diet.

That a child may be maintained at five weeks of age on a semi-solid diet with proper consideration of vitamines is evidence of the fact that this case has progressed to a normal state and is apparently healthy two and a half years after the onset of the acute hydrocephalus. Walking, talking and other signs of mental activity have progressed normally. There is no evidence of rickets and his physical appearance at the present time is one of normal health.

CASE V.—Baby, C. P., white, American, male, age two weeks. Born November 2, 1929, and admitted to Temple University Hospital November 21, 1929.

At time of birth presented a large growth (size of small orange) protruding from back in sacral region. This condition was congenital but no increase in the size of the mass was noted since birth. Child was a full term, normal, spontaneously delivered infant. No anesthesia or forceps used. Breast fed during past two weeks. No unusual complaints except for the myelomeningocele.

Family History.—Mother and father living and well. One sister age seven perfectly normal—living and well. During first pregnancy, mother had difficulty; required gas and forceps. Puerperal period two weeks. Was rather ill and lost weight and became progressively weak. Had frequent hemorrhages from uterus and it was necessary that she be under a physician's care.

Baby was breast fed during the first two weeks.

Physical Examination.—Male infant, well nourished, good color and weight 8 lbs. Head—contour normal. Sutures still open. Superior longitudinal, frontal, coronal and fronto-parietal sutures still not closed. Can palpate groove along all the sutures. Anterior fontanelle open—size of a quarter. No depressions or bulging of fontanelles. Posterior fontanelle small, practically not elicited. No signs of hydrocephalus. Eyes, ears, nose and mouth negative. Face good color and occasional erythematous blotches are present. No increase in cardiac-thymic dulness. Chest and abdomen practically negative.

Posteriorly, in region of the first, second and third sacral vertebræ and possibly the fifth lumbar, in the midline, is a peculiar protrusion—a growth the size of a small orange covered with skin and towards the periphery is noted a line of demarcation and change from skin to mucous membrane which has some slight tendency to ulceration. Quite vascular and no evidence of any pulsation or fluctuations. Probably a myelocele—lumbo-sacral region.

Progress.—On November 22, 1930, Doctor W. Wayne Babcock removed protruding sac measuring about 4½ by 3 inches and 3 cm. in depth. Area of medulo-vasculora, necrotic 3 cm. across. Few well formed pustules on adjacent skin. Cauda equina terminated about center of sac to which it was firmly adherent. Many fine nerve fibers in the wall of the sac. Opening of the bony canal 12 cm. in diameter opposite fourth sacral. Neural canal well formed. Reconstruction of the dural sac and bony canal.

Progress uneventful until November 27, 1930, when following was noted: Sphincter ani relaxed, protuberant, apparently without tone. Passage of feces at frequent intervals. Head reveals prominent superficial vessels of the scalp. Suture lines of the skull separated with excessive bulging of the fontanelles and over open suture lines. Line of incision is indurated, reddened and infected. Puriform material squeezed out through stitch abscess opening. The hydrocephalus and the proximity of the pus to the dura make the outcome of this case hopeless.

December 1, 1929: Right lateral ventricle tapped of fluid. 25 c. c. colorless fluid obtained.

December 5, 1929: Left ventricle tapped. 40 c. c. clear fluid removed. Internal strabismus present.

December 8, 1929: Skull assuming abnormal shape. Occipital area enlarging.

December 9, 1929: Fontanelles beginning to show excessive bulging. Child takes food normally. No cephalic cry. No symptoms or signs of meningitis. Little or no internal strabismus. Ventricular puncture with removal of 40 c. c. of fluid. Condition good following puncture.

December 17, 1929: Ventricle tapped. 30 c. c. of fluid removed.

December 22, 1929: Ventricular puncture performed. 45 c. c. fluid removed. Sutures still wide open.

December 26, 1929: Temperature has been normal for past few days. Wound of operation healed.

Laboratory Studies.—Blood count essentially normal. Spinal fluid examination revealed negative Wassermann, negative Kahn and colloidal gold 0000000000.

December 31, 1929: Patient transferred to the neurosurgical service of Dr. Temple Fay.

The details of the clinical observations covering a period of nine months on the neurosurgical service are shown in Fig. 6 which may be summarized as follows:

The child recovered from the meningocele operation performed in the second week and required repeated ventricular drainage because of definite signs of internal hydrocephalus which promptly followed the closure of the meningocele. The child was deteriorating rapidly and was referred to the neurosurgical service for treatment as a hydrocephalic at five weeks of age.

The baby was placed upon 12 total fluid ounces per day and in order to obtain the necessary calories, mashed bananas, mashed potatoes and other semi-solid foods were given in two ounce feedings every four hours through a wide nipple.

In spite of this rigid limitation of fluid, the child did well after an initial loss of weight. Sunlight and viosterol were given daily. The total fluid intake was raised to 20 ounces and on one occasion dropped to 14 ounces until the balance of intake and output was obtained. The child became definitely brighter. Ventricular drainage was not necessitated. The circumferential measurements showed 43 cm.; bitemporal measurement was 31 cm. in February of 1930. Following active dehydration, the bitemporal measurements decreased 8 cm. The circumferential measurement remained the same. The child steadily gained weight until the summer heat caused a rise in temperature and a marked loss of body weight due to excessive evaporation of fluid from the body surface and the lack of compensation for fluid permitted in the diet. The patient was sponged but the fluid level of intake was not permitted to be increased.

The weight loss occasioned in May, June and July was reestablished in August. The circumferential measurements increased 1 cm. The bitemporal measurement remained the same. There was no further sign of internal

hydrocephalus. The child progressed rapidly and at the end of one year in the hospital was discharged having reached within three pounds of normal age weight and having developed as normally in its mental processes as any hospitalized child could be expected to do.

Child was returned to the care of its mother who has maintained a strict limit of intake fluids to 20 ounces and at the present time, about two years after the period of observation, the child is walking, talking and gives evidence of being normal in all respects with the exception of a slight delay in the walking due to the disturbance of the muscles of the lower extremities secondary to the meningocele.

The above case illustrates satisfactory control of internal hydrocephalus by proper fluid balance and the prevention of progressive internal hydrocephalus with consequent mental deterioration.

That a semi-solid diet can be given even at five weeks of age is clearly evidenced by the progress in this case and the difficulties encountered were those occasioned by extremely hot weather when body fluid requirements entailed careful adjustment for the loss of fluids through the skin outlets. The weight curve apparently is a proper guide to this relation. It shows with rises of temperature a definite loss in body weight. The case further illustrates the advantage of preserving the cerebral and mental activity in such a case even at the risk of physical impairment of growth which, fortunately, has not shown itself in any way during the three years covering this observation.

These three cases illustrate the pathology of this group; two of known etiology and one of doubtful etiology (still living and improving), where acute signs of mental deterioration were checked temporarily in two, but with progression as the cycle of attacks increased and the periods of pressure were prolonged. The third case represents one of four similar instances with improvement upon limitation of fluid and diet, after withdrawal of excessive spinal fluid and the use of the encephalogram.

Group III.

ACUTE CEREBRAL HYDRATION STATES ASSOCIATED WITH RAPID MENTAL FAILURE.

Eclampsia, status epilepticus and acute alcoholic wet-brain present crises in which mental activity is rapidly lost, and the individual enters a phase of dull, drowsy confusion or stupor. In this group,

direct operative exploration and observation have revealed during the past three years intensely edematous conditions of the brain.

In the eclamptic the brain is grey-white, avascular, and swollen, with marked increase in the amount of fluid in the subarachnoid space, but with only a small amount of subdural fluid obtainable. The structures remind one of soggy bread, and so intense is the cortical anemia that the brain appears grey-white, streaked by a few arterioles dispersed over the convolutions. The results of rapid dehydration, with withdrawal of spinal fluid and denial of all food and fluid in this group, have been reported (Arnold and Fay).[1] and the prompt improvement in the patient's mental status and symptomatic relief are discussed in detail in this paper.

With the withdrawal of spinal fluid, the intravenous use of glucose and limitation of fluids, accompanied by purgation, there is a rapid return to mental activity within four to six hours, and normal cerebral manifestations return within 24 to 48 hours after the withdrawal of excessive amounts of spinal fluid and cerebral edema.

In several cases of status epilepticus, dehydration and spinal drainage have been effectual, but occasionally the cerebral signs have persisted. Direct exploration of the cortex has revealed a large accumulation of *subdural fluid* as well as an increase in subarachnoid fluid, caught in the tissue spaces and not removed in spite of the measures of dehydration and spinal drainage. Autopsy has demonstrated in two cases that cerebral edema has persisted in spite of the most active measures of dehydration and direct cortical drainage. Marked improvement has been accomplished in a number of such cases by methods directed toward the removal of spinal fluid as well as *subdural fluid,* when necessary.

In the posttraumatic and alcoholic wet-brains, a similar state exists excepting that large amounts of subdural fluid are usually obtained from both cortical surfaces and this is not drainable by spinal puncture and can only be removed by trephine of the skull and directly opening the dura. Da Costa [2] has pointed out the necessity for this direct drainage in the treatment of such severe cases.

This group represents the acute phases of mental loss followed by prompt recovery where adequate measures are effectual.

In two cases of subdural hematoma (400 to 600 cc. volume respectively) *with slight increased pressure* (12 mm. Hg.) where the hematoma had been present seven months and fourteen weeks, respectively, marked mental deterioration was present. After removal of the subdural clot (in one instance extending from the frontal to the occipital area on the left, and in the other a similar distribution on the right), the patients made a prompt and rapid return to mental activity.

CASE VI.—Mr. D. H., white, American, male. Grocer. Age 65.

Referred by Dr. W. H. Conway to Dr. Temple Fay.

Admitted to Temple University Hospital with chief complaints of terrific headache, dizziness, staggering to left and drowsiness which followed automobile accident ten weeks prior to admission. History of unconsciousness for 30 minutes at time of accident. Patient hospitalized eight hours. Had bump on right side of head. Day before admission to Temple University Hospital had urgency and incontinence.

Examination revealed that patient was dull, apathetic, distinctly deteriorated. Used his right arm and hand more than the left. Slight asymmetry of face with relaxation on the left. Slight fullness and relaxation of muscles of the tongue. Closed eyes firmly but muscle tone changed on left. Contractions seemed firmer on the right. Left pupil slightly larger than right. Lip movements in speech slow; slight absence on left. Hypertonia in left arm. Reflexes increased on left. Slight but definite atrophy of left arm, forearm and hand muscles.

Eye examination was negative. The Barany examination was positive for supratentorial lesion on left.

Progress.—Patient was somewhat disoriented for time and place. There was definite slight spasticity of left arm and leg.

Nine days after admission a right fronto-parietal craniotomy was performed. Subdural hematoma found encapsulated in sac. This was freed from the dura and then from the cerebral cortex. Bleeding from several large surrounding veins was controlled. Catheter drain was left in wound and the operation completed.

Patient was in moderate shock when returned to ward. In first 24 hours there was considerable cerebrospinal fluid drainage from wound. Patient responded normally to questions and was greatly improved mentally. Became bright, alert and carried on spontaneous conversation. Appeared to have no memory defect after operation.

Four days later patient developed signs of acute pulmonary edema and died apparently from cardio-respiratory failure.

Case VII (J. D.) 18 months after operation was pursuing his normal activities although a return of emotional instability, depression and mental hebetude required withdrawal of fluid which had

formed in the cavity produced by the clot three weeks after operation, and this was followed by a prompt return of his mental activities.

CASE VII.—Mr. J. D., white, American, farmer. Age 40.

Admitted to Temple University Hospital, service of Dr. Temple Fay, November 26, 1930, five months after receiving a severe blow to head and face which caused no immediate symptoms. A definite change in personality occurred, followed by left parietal headaches, nausea and vomiting. Hospitalized twice in Trenton totalling 11½ weeks, but symptoms progressed and patient developed attacks in which he could not speak and appeared stuporous. During the attacks his temperature rose as high as 103° F. Attacks lasted about 36 hours. During and between the attacks, he had vomiting spells, some projectile in character. Appeared disoriented at times.

Physical and neurological examinations revealed slight depression in left temporal area. Tenderness to percussion in this area. Palate raised bilaterally, but more on right. Vision impaired. Pupils and palpebral fissure both greater on right than left. Pupils reacted promptly to light and in accommodation. Apparently some facial weakness on right. Had difficulty in deglutition. No other positive findings.

On admission to Temple University Hospital patient was definitely disoriented. Marked tendency to sleep though easily aroused. Mentally confused.

Four days after admission spinal tap performed. Initial pressure 12 mm. Hg. 5 c. c. clear, colorless fluid was removed. Patient mentally clearer following tap.

X-ray (Dr. W. Edward Chamberlain) showed pineal shift to the right. Diagnosis: Left subdural hematoma (chronic).

On December 1, 1930, an exploratory craniotomy in the left temporo-occipito-parietal area was performed. An extensive organized hematoma about 2 inches in thickness extending from the frontal pole to the occipital lobe was found. The cystic clot was opened and drained and the clot wall carefully removed from the cortex. The hematoma measured 4 cm. in width by 10 cm. in length. A drain was left in the cavity occupied by the clot and the patient then returned to his room in satisfactory condition.

Post-operative condition remained excellent. Patient rational after return from operating room. Speech returned in 24 hours. Mental activity was greatly improved.

On the sixth day following operation, the temperature again became elevated and the patient irrational and apathetic. The posterior limb of the cranial flap was elevated and the dura incised. About 3 ounces of yellowish fluid was sucked out. After complete drainage of the cavity it was noted that the brain substance had partly refilled the space occupied by the large hematoma.

Following this second removal of fluid, the patient rapidly improved. The weakness on the right side entirely cleared within five days and speech returned to a point where he showed no signs of aphasia. He was optimistic and bright and was discharged on December 21, 1930, in excellent condition.

He was placed on a strict fluid balance, dry diet, with an intake of 30 ounces of liquids permitted per day.

Subsequent examinations have shown that he has gradually returned to his former mental state and is now undertaking the activities of his farm without difficulty. Occasionally there are periods of emotional depression but his wife states that there are no signs of his dull and listless state which characterized the period during which the hematoma was present. She believes his mental activities are as acute as formerly and neurological examination two years after discharge revealed no signs of asphasia or mental deterioration or positive neurological evidence of his former lesion.

Case VI (D. H.) showed prompt return of consciousness after operative removal of the clot, but eventually succumbed to pneumonia, although mentally alert up to the time of this secondary complication.

The above group serves to illustrate the fact that where cerebrospinal fluid volume has increased at the expense of blood volume, thus removing necessary blood from the cortical circulation, signs of mental deterioration appear, either in their acute or chronic phase; that with the withdrawal of the abnormal fluid or clot volume, there is a return of blood to take its place, and with the return of cerebral circulation there is better availability of oxygen, consequently there follows improvement in cortical function and mental activity.

Group IV.

POSTTRAUMATIC NEUROSIS.

In the 298 consecutive cases of cerebral trauma coming under my care during the past three years, 46 per cent of which had subarachnoid hemorrhage, the patients have been drained of their excess of spinal fluid and maintained after their discharge from the hospital on 32 ounces of fluid intake and a dry diet. This has resulted in 94 per cent of this series being free from the usual posttraumatic sequelæ such as dulness, loss of attention, inability to concentrate, headache, vertigo and vague feelings of malaise. Formerly 40 per cent of the posttraumatic group have given evidence of these symptoms which led gradually to their withdrawal from economic and social affairs, and consequent low-grade type of mental deterioration.

Many posttraumatic (so-called) " neuroses " have been observed after complaining of the above symptoms for months or years, and

with spinal fluid drainage, including encephalography for confirmation, and the proper balance of fluid in the diet, as well as liquid intake, they have shown striking improvement in their former symptoms, so that there was an apparent increase in attention, interest, memory, psychomotor activity, associated with lessening of the headache and gradual readjustment to some improved economic and social phase, in the majority of cases.

The methods of treatment and results obtained are discussed in full elsewhere [3, a, b] and need no further elaboration in this presentation.

Group V.

EPILEPTICS PLACED UPON DEHYDRATION ROUTINE.

Over 300 cases of chronic epileptics have been included in this analysis and those in which actual dehydration was accomplished by proper balance of fluid and diet (with consequent loss of body weight, averaging from 5 to 11 pounds, which is necessary in order to produce a diminution in the fluid tissue reservoir of the body), have shown striking improvement in their mental attitude and in only four instances during the past eight years has there been evidence of progressive mental deterioration, whereas the majority of the cases have actually improved in their mental responses and a few remain arrested as far as the deterioration is concerned. In this group, improvement has been evidenced by an increase in psychomotor activity, improvement in attention, concentration and memory, as well as a decided relief from the post-epileptic phase of stupor, dulness and mental hebetude, so common throughout the group evidencing major convulsive seizures.

In the mentally deteriorated groups of epileptics, the improvement noted is hardly to be desired, but gives evidence of increased instinctive cunning and destructive ability. The patients when properly dehydrated and maintained under strict supervision (which is almost impossible excepting under the most ideal circumstances) are released from their dull, passive states of inactivity. They become mischievous, destructive and quarrelsome in their responses; although distinctly antisocial, nevertheless, representing an increase in psychomotor activity of the primitive type and offering further difficulties in the process of management.

One cannot expect to improve an intellect which has had little or no opportunity for development or to obtain improvement in social relationships when training and regard for these factors have been deficient.

The evident improvement in those cases where intellectual levels have not been impaired and where social behavior is well established, indicates that the benefit in response to dehydration is a matter of enhanced inhibitory control rather than any change in primitive instincts.

The work of Whitney and Hunsicker [4] indicates the response which may be expected from the lowest type of mentally deteriorated epileptics, under the most rigid institutional supervision. Their careful studies clearly show that the I. Q. is not improved during effective dehydration, as there has been no additional intellectual training to offer this group. The tests on performance showed definite improvement, and these may be considered in the light of some improved psychomotor activity.

PART II.

The craniovertebral cavity represents a total fixed volume in cases where the fontanel is closed and no surgical decompression has been accomplished. It is evident that the container cannot expand momentarily and requires a prolonged and gradual process in cases of hydrocephalus where the structures have once closed. If the craniovertebral cavity were completely closed, and filled with fluid, it would be impossible to withdraw fluid from this container without introducing an equal amount of some other volume, in the same way that it is impossible to withdraw fluid from a rigid container such as a corked bottle, filled to capacity, without introducing air or some other volume displacing agent.

The craniovertebral cavity is not entirely closed, as the arterial inlets and venous outlets permit shifts of blood volume to occur. Therefore when spinal fluid is withdrawn from this cavity, a similar volume of blood must enter in order to permit the proper displacement to occur, and as long as the arteriovenous outlets are open, negative pressure would be immediately compensated for by an inflow of blood.

We must consider the act of spinal drainage or withdrawal of spinal fluid by any means whatsoever, as associated temporarily at least, with an equivalent inflow of blood volume. When spinal fluid is under pressure within the ventricles such as is seen in acute hydrocephalus, it is evident that increase in the amount of spinal fluid has displaced some other volume, because if the craniovertebral cavity has not enlarged, there is no possibility of increasing the total fixed volume, and the other volume components of the craniovertebral cavity must yield before the increase of spinal fluid volume. This is usually at the expense of brain substance when compression is prolonged. The loss of brain substance is in the end secondary to compression anemia, as it cannot escape the active pressure created by the vascular and spinal fluid circulation. The surplus of venous blood in the perivertebral sinuses and large cortical sinuses may yield, to a certain degree, without disturbing the efficiency of cerebral circulation, so that we may encounter the situation in which 10 to 20 cc. of spinal fluid volume have been added and 10 to 20 cc. of blood subtracted, without change of the total volume and without change in intracranial pressure. Larger amounts in the form of blood clots, tumor masses, etc., have clearly demonstrated that such changes can occur without rise in pressure and must be compensated for by an equal volume of some other component. Pressure readings only indicate the resistance of one volume component toward another; that is to say, pressure, in the last analysis, is the force of resistance measured in terms of mercury or water, which is actively demonstrated by the components within a closed or partly closed system. As fluids are incompressible, it is evident that when one volume increases it must be at the expense of another. (Fig. 7.)

If spinal fluid pressure is high such as we find in internal hydrocephalus, it merely indicates that there is an active and determined resistance on the part of blood volume (blood pressure) not to yield, as is clearly evident if the individual should suddenly succumb to a cardiac failure. Intracranial pressure would and does fall to zero immediately. It is the active presence of the circulating blood volume which produces the resistance against the accumulation of cerebrospinal fluid, and when the cerebrospinal fluid is withdrawn such as by ventricular puncture, the escape of this fluid under pressure only represents the inrush of blood to take the place of fluid

expelled, and the volume of spinal fluid expressed represents the amount which blood volume can replace until the limits of vascular compensation have been reached (dural elasticity (Weed) included).

This principle is so well known in neurosurgery that rapid withdrawal of ventricular fluid, under high pressure, is known to be disastrous (through the occurrence of spontaneous hemorrhage in

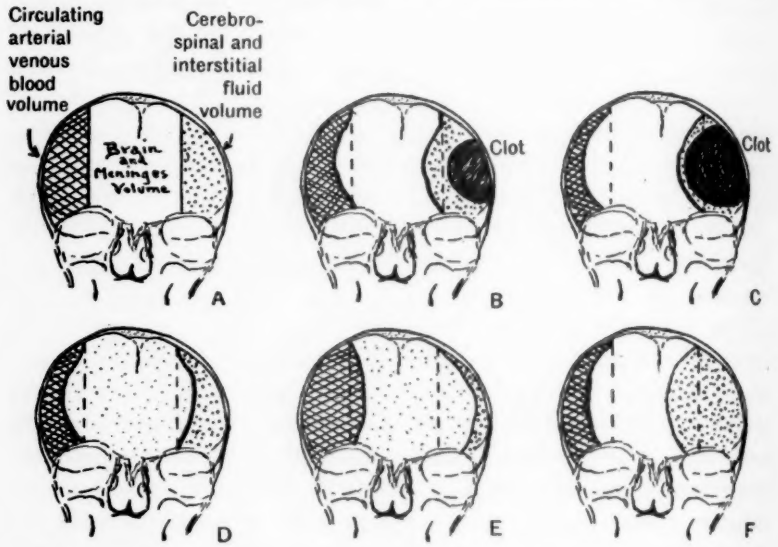

FIG. 7.—Changes in volume relationships which may occur within the range of compensation without giving rise to an increase in intracranial pressure. The addition of a new volume component such as subdural hemorrhage may arise without an increase in intracranial pressure, if a similar volume, or one or more of the components of the cranial-vertebral cavity yield to an equal degree. The volume shifts are of profound importance when blood volume is reduced by excess of spinal fluid volume, intrinsic swelling of brain tissue or new additions such as hematomas or tumor masses. Spinal pressure readings only indicate the resistance of one volume to another and increase in pressure can only be expected when the limit of compensation for adjustment of one volume to the other has been reached and there develops active resistance against disproportion of the normal ratios of the cranial-vertebral cavity components.

tumor masses, when the inrush of blood is unchecked, and not gradually permitted to occur). The surgeon in the presence of such high pressure reduces this pressure slowly and gradually for fear of a spontaneous rupture or petechial or massive intramedullary hemorrhage which may occur as blood again returns to the pathways from which it had formerly been expressed.

If the volume of spinal fluid can be reduced by ventricular puncture, spinal drainage, purgation, dehydration or any means jus-

tifiable to the case in question, it is immediately compensated for by a replacement of blood volume, which represents in all but a few instances, increase in cerebral circulatory efficiency; increase in oxygen available, and consequent improvement in tissue function which in terms of mental activity may be noted by better sensory and psychomotor responses and the generalized condition described as improved mentality.

With this concept, it is evident that the results noted above appear to be secondary to improved cerebral circulation and the improvement in cerebral circulation, with its consequent improvement in oxygenation, is dependent upon a wide variety of factors, but in this group of cases there seems to be the only single factor concerning the volume of cerebrospinal fluid, whether withdrawn during acute periods by direct ventricular tap, spinal drainage, or the use of hypertonic solutions, or in the more delayed and chronic groups by the strict balance of fluid and diet, to prevent periods of cerebrospinal fluid volume increase at the expense of blood volume, which when expressed in various degrees may be associated with cerebral functional deficiencies and chronically result in mental deterioration.

Although spinal pressure does not indicate the possible shifts that may occur in the volume relationships and although we find many cases where cerebrospinal fluid pressure is normal, in the presence of mass lesions (indicating that such displacement has been compensated for), nevertheless, studies based upon a large number of cases tend to show certain average pressures which may be expected in these groups.

In over 3000 lumbar punctures the normal spinal fluid pressure, in my opinion, has been considered as 8 mm. Hg. (the range of normal lies between 6 and 10 mm. Hg.). In my experience and opinion, patients with 10 mm. Hg. of pressure or above, have shown by encephalography that there is demonstrable pathology of the brain, whereas in 467 encephalograms undertaken during the past five years, the normal brain patterns have been associated with from 7 to 9 mm. Hg. of pressure in the vast majority of cases. (Table I.) Hence, I am confident that where pressures above 10 mm. Hg. are encountered (when carefully taken in the horizontal position without straining or movement on the part of the

patient and checked after the coughing and straining responses, as well as by *encephalography*) a definite pathological change can be demonstrated which indicates that the patient cannot be considered as entirely normal. Although the range of pressure used by others (Cobb and Fremont-Smith) is in terms of millimeters of water, the range of normal which they accept is the equivalent of 7 to 14 mm. Hg. I disagree with the wide limits of normal adopted by these investigators because of the numerous cases of brain tumor,

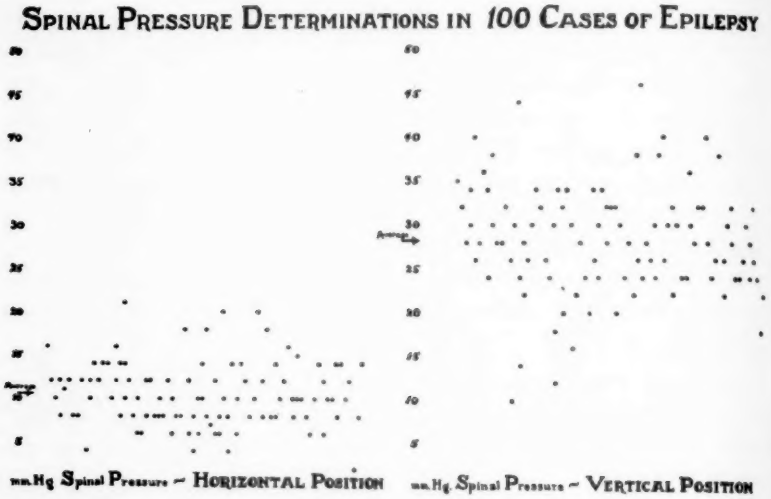
SPINAL PRESSURE DETERMINATIONS IN 100 CASES OF EPILEPSY
mm.Hg Spinal Pressure – HORIZONTAL POSITION
mm.Hg Spinal Pressure – VERTICAL POSITION

FIG. 8.—Spinal fluid determination on 100 epileptics in the horizontal and sitting positions indicating that 67 per cent of the cases showed pressures of 10 mm. Hg. or above in the horizontal position. The values of pressures in the sitting position are not constant because the pressure varies somewhat according to the length of the column of fluid in the individual's spinal canal and this varies with the height of the patient.

subdural hemorrhage, cerebral trauma and various other pathological states, where pressures have been recorded between 12 and 14 mm. Hg. and cannot escape the careful attention of observers or be included in the " normal " range. Fig. 8 represents the spinal fluid pressure in millimeters of mercury in 100 cases of epilepsy, in the horizontal and sitting positions, the readings being made on each case, first in the horizontal position and then immediately following this recorded in the sitting or vertical position. The average horizontal pressure was 10.55 mm. Hg. whereas the average sitting pressure was 28.29 mm. Hg. Fig. 8A represents

the same series of cases in their relationship to my accepted normal range of intracranial pressure. As will be noted, 8 mm. Hg. was the most frequent pressure recorded but the majority of cases (67 per cent) registered pressures of 10 mm. Hg. or above. As previously stated,[5, a, b, c] in my opinion, the majority of epileptics fall in the top-normal pressure groups, and I consider pressures of 12 mm. Hg. or over as distinct signs of low-grade increased intracranial pressure.

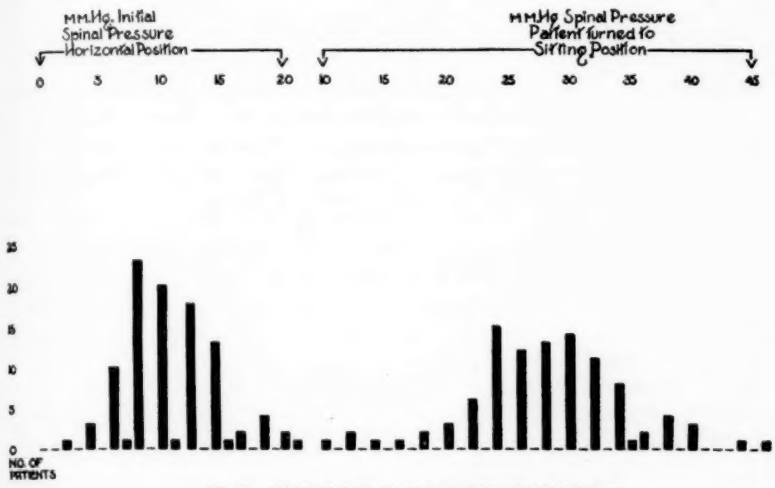

FIG. 8A.—100 cases of epileptics grouped in relation to the spinal fluid reading obtained in the horizontal and sitting position. Note that the largest number of cases in any one group show 8 mm. Hg. pressure in the horizontal position, and that the majority of cases are to be found with pressures of 10 mm. Hg. or above in the horizontal position.

It is interesting to note (Table I) the comparison of pressure in various groups. The chronic posttraumatic group shows an average horizontal pressure of 9.33 mm. Hg. and 27.1 mm. Hg. in the sitting position. In a third group of miscellaneous neurological conditions, in which the patients presented vague symptom-complexes, the average horizontal pressure was 9.6 mm. Hg. and the average sitting pressure was 26.7 mm. Hg. In my group of brain tumors, spinal puncture was only performed where marked signs of intracranial pressure were not present, because of the danger associated with spinal puncture in such cases. However, in those cases of proved brain tumors, where few or no signs of increased pressure

existed, an encephalogram was obtained. In the horizontal position they gave an average pressure of 15.44 mm. Hg. whereas, the pressure in the sitting position after drainage of spinal fluid to 8 mm. Hg. (precaution against foraminal hernia when patient placed in the upright position) showed 27 mm. Hg. The sitting position pressure, of course, is not as high as it would have been if the patient had been allowed to assume the upright position with drainage for correction of the increased pressure noted in the horizontal position.

Group 5 represents brain tumors in which encephalogram was

TABLE I.

AVERAGE INITIAL SPINAL PRESSURES IN THE HORIZONTAL AND SITTING POSITIONS AS DEMONSTRATED IN THE FOLLOWING FIVE GROUPS:—(1) EPILEPSY, (2) CHRONIC POSTTRAUMATIC, (3) MISCELLANEOUS CASES, NOT INCLUDING BRAIN TUMORS, (4) BRAIN TUMORS AND DEFINITE SUSPECTS (DIAGNOSTIC TAP ONLY), AND (5) BRAIN TUMORS.

Group classifications.	Average Initial spinal pressure, horizontal position in mm. Hg.	Average spinal pressure, patient in sitting position in mm. Hg.
ENCEPHALOGRAMS.		
No. 1. Epilepsy	10.55	28.29
No. 2. Chronic Post-traumatics	9.33	27.1
No. 3. Miscellaneous Cases (not including Brain Tumors)	9.6	26.7
No. 4. Brain Tumors and Definite Suspects	15.44	27.0
DIAGNOSTIC TAP ONLY.		
No. 5. Brain Tumors	16.9	....

not felt to be advisable, and where in 16 cases the average horizontal pressure was found to be 16.9 mm. Hg.

The above determinations, covering over 300 observations, carefully checked by encephalography, clearly indicate that pressures obtained in the brain tumor and epileptic groups are higher than those obtained in the posttraumatic and miscellaneous, and the pathology demonstrable by encephalography confirms the opinion that when spinal fluid pressure is 10 mm. Hg. or over, it may be considered as the first evidence of increased intracranial pressure, the pathology of which is usually demonstrable and clearly indicates that the acceptance of such wide levels of "normal," as adopted by Cobb and Fremont-Smith [6] is not justifiable in that their cases have not been confirmed by encephalography and operative means.

According to their limits of "normal," my brain tumor series would be considered just above their top-normal pressure, and it is obvious that the values adopted by them will require further refinement.

A confusing point which has aroused much discussion is the attempt to compare spinal fluid readings, obtained from a simple "U" tube mercury manometer with those of water manometer readings adopted by some. The spinal fluid pressure readings made by the Fremont-Smith-Ayer type of water manometer and published prior to April 1931, were uncorrected for capillarity, and hence when compared with mercury gave abnormally high readings.

In my opinion the water manometer is of value in detecting small variations in pressures when comparative values are being recorded for determinations of spinal cord tumor or block by the Queckenstedt method, but any instrument which will require the introduction of such errors, including loss of spinal fluid into the manometer itself, should be discarded as a basis for establishing normal pressure readings, and the standard of mercury as a basis for these determinations cannot be displaced by such unscientific instruments.

Fig. 9 indicates the relative values of mercury and water as they should occur when computed by their difference in specific gravity. The capillarity error in the water manometer has been corrected as shown in this chart, and the abnormally high readings prior to April 1931, indicate the misleading basis for conclusions adopted prior to the recognition of this error.

Objections have been raised as to the theory of fluid limitation and dehydration, by Cobb and Fremont-Smith.[6, 7, 7a] The basis for this attack rests upon seven cases presented by Fremont-Smith and Merritt[7] in which dehydration was attempted. "Fluid" was restricted to 100 to 350 c. c. per day. The authors noted no change in spinal fluid pressure or in the volume after five days,[7a] although the data presented clearly indicate that in six out of the seven cases the patients were on an unrestricted diet and received sufficient fluid so that they were able to pass 1100 to 3650 c. c. of urine (approximately 4 to 7 pounds) and in spite of this unexplained increase in fluid elimination, the patients' weight did not change during the five day period, but in one case actually increased 1.5

COMPARISON MERCURY AND WATER READINGS.

Spinal Fluid Pressures.

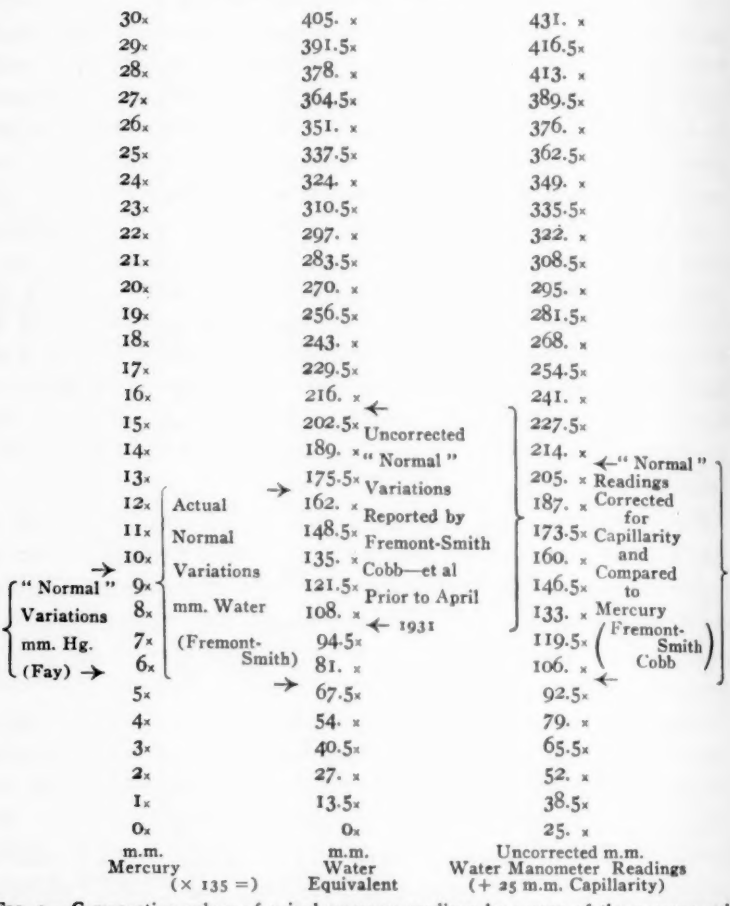

Fig. 9.—Comparative values of spinal pressure readings by means of the mercury and water manometers. Note column 2 represents the exact water equivalent for mercury and indicates the level of normal (100 to 200 m.m. of water) attributed by Fremont-Smith, although reported values prior to April, 1931, in terms of mercury and uncorrected for capillarity caused confusion because of the necessarily high mercury equivalents.

Column 3 represents the readings on the present water manometer in terms of mercury equivalent when corrected for 25 mm. of capillarity.

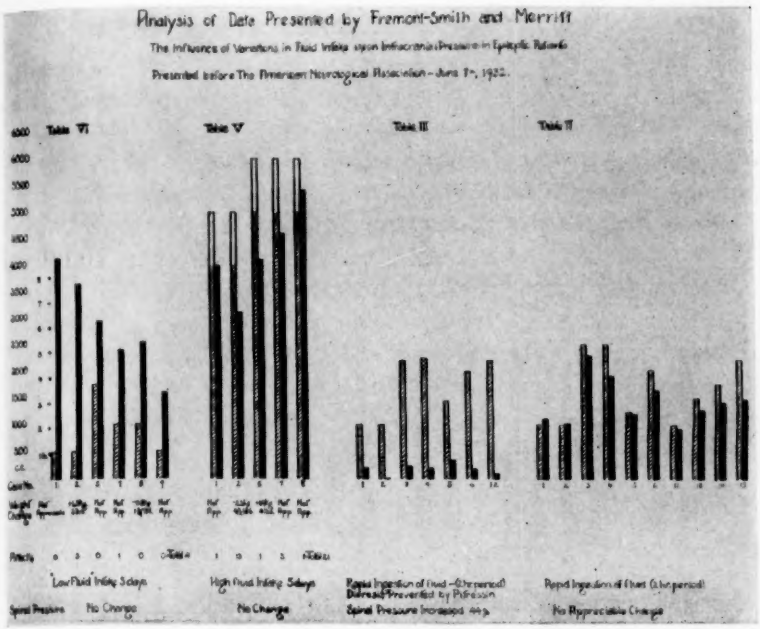
Analysis of Data Presented by Fremont-Smith and Merritt
The Influence of Variations in Fluid Intake upon Intracranial Pressure in Epileptic Patients
Presented before The American Neurological Association - June 7th, 1932.
Table VI
Table V
Table III
Table II
Low Fluid Intake 5 days
High Fluid Intake 5 days
Rapid Injection of Fluid - 2 hr. period
Diuresis Prevented by Pitressin
Rapid Injection of Fluid 2 hr. period
Spinal Pressure No Change
No Change
Spinal Pressure Increased 44%
No Appreciable Change

FIG. 10.—Analysis of data presented by Fremont-Smith and Merritt upon which they base their attack on the effectiveness of dehydration in relation to spinal fluid pressure. Note Group 1, Table VI, comprises the cases in which they limited fluid intake (shaded column) and claimed no change in intracranial pressure or volume during the five-day period of low fluid intake. The black columns represent output of patient during this period and clearly show that fluid was obtained from other sources (diet uncontrolled) as no appreciable change in body weight occurred. In fact, Case 2 shows a gain of 3 lbs. in body weight. (One case lost 1¾ lbs.) The basis for their conclusion that low fluid intake does not effect intracranial pressure or volume is unfounded based on this experiment because the patients received sufficient fluid to maintain their body needs including the amount lost by skin, breath and bowels and still showed a marked excess in output (1100 to 3650 c. c.) in spite of so-called low fluid intake.

Group 2, Table V, indicates a period of forced fluid intake (shaded column) and indicates again no appreciable change in body weight, but the fact that the patients eliminated fluid almost as rapidly as it was ingested. Hence no storage of tissue fluid and no change in spinal pressure. Note, however, total convulsive seizures during low fluid intake was 4, whereas, during high fluid intake period 21 convulsions were recorded.

Group 3, Table III, shows the effects of rapid ingestion of fluid over a two-hour period when retained in the body by means of renal suppression (injection of pitressin). Note spinal fluid pressure increases 44 per cent when acute retention of body fluid occurs.

Group 4, Table II, indicates a two-hour period of forced fluid intake (shaded columns) with output almost proportionate to intake indicating ample compensation for elimination and little evidence for tissue fluid storage (no weights given). No change of intracranial pressure noted.

Above data clearly shows that retention of body fluids and consequent gain in weight is associated with a rise in intracranial pressure; that when intake and output are properly balanced, little or no change in spinal pressure occurs. As no dehydration (loss of body weight) was obtained in this series, their conclusions regarding low intake of fluids are not acceptable because of uncontrolled fluids in the diet indicated by excessive output without loss of weight.

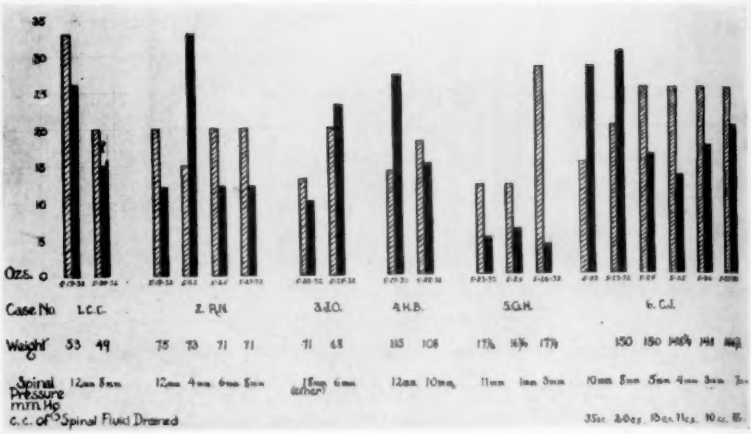

FIG. 11.—Controlled and effective dehydration (patients on service of Dr. Temple Fay). Intake and output record of cases placed on strict dehydration indicating definite loss of body weight as well as gradual decrease in spinal pressure. Note that in Case 6, readjustment of spinal pressure occurs at low levels of body weight after intense period of dehydration has been adjusted.

kilograms (3 pounds) and this measurable amount of fluid excreted, does not include the large amount lost by skin, breath and bowels.

In other words, if the patients showed no loss in weight (one pint weighs approximately one pound), during this period, it is evident that they did not subtract fluid from the tissues of the body, as this loss would have been recorded in the patient's weight. It is further evident that the patients received through the uncontrolled diet, sufficient fluid to meet their body needs, and be able to discard 1100 to 3650 c. c. of fluid (approximately 5 to 7 pounds) besides, and this these investigators claim is fluid limitation to produce dehydration. (See Fig. 10 for analysis of their data.)

Cobb states [6] that he believes from 600 to 1000 c. c. of spinal fluid are produced in the human being per day, and denies that spinal fluid volume or pressure can be reduced by dehydration methods which we have employed. (See Figure 11, Case 6, also Table II.)

I have clearly demonstrated,[3, a, b] that certain posttraumatic cases placed on 20 ounces of fluid per day, with daily spinal drainage, produced little or no fluid after the second day. In hydrated types, fluid may be obtained in small quantities up to the third and fourth day, but if rigid dehydration is maintained and daily spinal drainages instituted, a point is reached in which the pressure is low, and spinal fluid cannot be obtained in the horizontal position. Irrespective of Cobb's doubt of this factor, I have over 100 of such observations in a series of 298 consecutive trauma cases, and this is sufficient to convince me that strict dehydration produces a state in which the spinal fluid reservoir is not completely refilled after excess of body tissue fluid has been withdrawn. I do not deny the possibility of a continual turnover in the cerebrospinal fluid system, not obtainable by drainage, but state emphatically that spinal fluid pressure may be reduced and spinal fluid volume which is obtainable, curtailed, if proper dehydration be instituted in these cases.

It is further demonstrable that if the patient is placed on 30 ounces of fluid, 45 to 60 c. c. of spinal fluid may be obtained with each daily drainage, indicating that the spinal fluid reservoir has been replenished and at least this amount of extra fluid is obtainable daily on a 30 ounce level of intake, where it is not

TABLE II

Analysis of Patient's Weight, the Intake, Output and Spinal Pressures with the Amount of Spinal Fluid Obtained in a Strictly Dehydrated Group.

Dates	May	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Case 1. C. C.	Weight	53	53	53	52	52	52	52	52	51	51½	..	53	54	..	54¾	..	..	54	53	..	..	..	..	..	49	..	..
	Intake	20	20	20	20	20	20	20	17	17	31	30	33	30	25	24	25	23	26	24	21	25	20	20	20	20	20	..
	Output	14	11	11+	12	19	9+	18+	19	15	29	19	26	15+	21	21	30	22	27	20	10+	15	13	?	13+	20	20+	..
	Spinal pressure	..	..	..	..	..	..	..	..	..	..	..	12 mm. Hg.	..	..	..	..	..	..	..	..	..	..	8 mm. Hg.	..	..	..	..
Case 2. R. N.	Weight	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	75	..	..	73	70½	71	71½	71	70½	70½
	Intake	..	..	..	..	..	..	..	..	..	..	..	..	38	35	33	20	16	20	15	15	20	20	20	20	20	..	..
	Output	..	..	..	..	..	..	..	..	..	..	..	..	13	20	17	12	12	16	14	33	20	20	12	16	12	..	..
	Spinal pressure	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	12 mm. Hg.	..	..	..	4 mm. Hg.	..	..	6 mm. Hg.	..	8 mm. Hg.	..	..
Case 3. J. O.	Weight	..	..	..	..	..	..	..	..	..	..	..	..	..	71½	..	..	..	..	71	..	.. P.S.P+	69	68	..	66½	..	..
	Intake	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	13	20	33	20	20	..	..	..	..
	Output	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	10	18	21	15	23	..	..	..	..
	Spinal pressure	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	18 mm. Hg. (ether)	..	..	..	6 mm. Hg.	..	..	..	..
Case 4. H. B.	Weight	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	115	..	..	..	..	..	111 P.S.P+	109 P.S.P+	108¾	108	..	..
	Intake	..	..	..	..	..	..	..	..	..	..	..	..	..	..	10	14	20	20	20	20	20	30	29	36	18	18	..
	Output	..	..	..	..	..	..	..	..	..	..	..	..	..	..	10	32	19	13	21	8	15	15	19	18	10	15	..
	Spinal pressure	..	..	..	..	..	..	..	..	..	..	..	..	..	..	12 mm. Hg.	12 mm. Hg.	..	..	..	..	..	..	..	..	..	..	10 mm. Hg.
Case 5. G. H.	Weight	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	17½	16¾	17⅛	16¾	17
	Intake	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	30	12	12	12	12	33	10	..
	Output	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	?	3+	?	5	6	4	4	..
	Spinal pressure	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	11 mm. Hg.	..	1 mm. Hg.	3 mm. Hg.	..	4 mm. Hg.
Case 6. C. J.	Weight	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	150	150	148¼	148	146½	..
	Intake	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	15	20	25	25	25	25	..
	Output	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	28	30	16	13	17	20	..
	Spinal pressure	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	10 mm. Hg.	8 mm. Hg.	5 mm. Hg.	4 mm. Hg.	3 mm. Hg.	7 mm. Hg.	..
	Spinal fluid drained	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	35 cc.	20 cc.	13 cc.	11 cc.	10 cc.	15 cc.	..

obtainable on a 20 ounce level, the case being strictly controlled so far as diet, enemas and other fluid factors are concerned.

That spinal fluid is produced in such a large quantity (600 to 1000 c. c. daily) suggested by Cobb, is open to question in my mind, because in my experience when repeated ventricular drainage has been required each 24 to 36 hours, in cases of acute hydration (hydrocephalus or cerebellar tumors) only 60 to 180 c. c. of ventricular fluid have been obtained. In a case of subdural fluid (acute alcoholic wet-brain) I have obtained as high as 280 c.c. in 24 hours of continuous drainage. Encephalography requires complete drainage of cerebrospinal fluid; from 100 to 360 c. c. have thus been obtained (115 to 130 c. c. normal quantity). Reexamination by x-ray shows that it requires from 24 to 72 hours for the air to become absorbed and the spinal fluid to refill the entire subarachnoid system.

With the evidence now at hand, it seems doubtful if even 300 c. c. of spinal fluid are produced normally, daily, and hence the "turn over" would amount to 12 c. c. per hour or three drops per minute. This could hardly be expected to produce a "flow" of spinal fluid of measurable degree as claimed by Cobb,[6] because of the wide absorption field in the spinal canal as well as over the surface of the hemispheres, preventing any definite direction of the current flow, and this agrees with the findings of E. Sachs.

The cerebrospinal fluid system is one of the body fluid (Fig. 12) reservoirs and may be considered similar to the interstitial spaces, according to Gamble.[8, a] The subtraction of fluid from the body tissues affects this reservoir, whether promptly by the use of magnesium sulphate as demonstrated by Weed,[9, a, b, c, d, e] or more gradually by the restriction of fluid intake below the level of body requirements, and where increased elimination is present produces consequent loss of body weight. If one is to deny the effects of dehydration by the gradual method of fluid limitation one must also deny the effects of hypertonic solutions established by Weed,[9, a, b, c, d, e] who's observations have been generally accepted.

PART III.

The cases presented in this paper illustrating some of the factors concerned in acute mental deteriorating processes, indicate that the volume relationships between blood, spinal fluid or mass lesions are

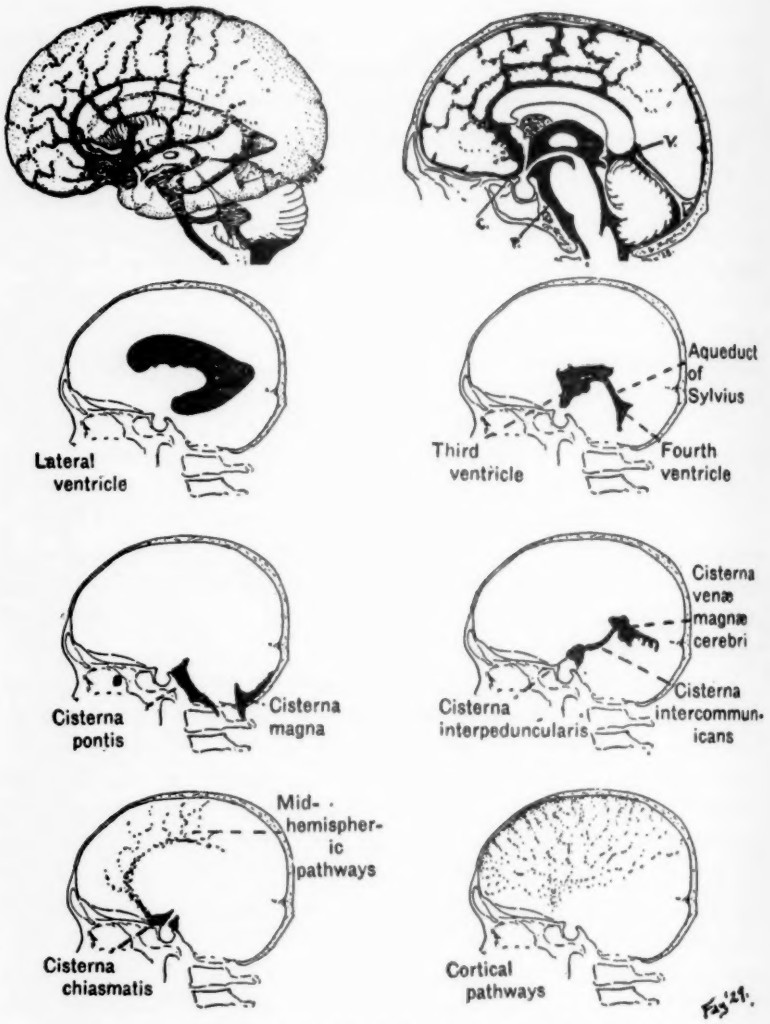

FIG. 12.—A diagrammatic relationship of the spinal fluid pathways to the surface of the brain. In the posttraumatic the greatest cerebral atrophy occurs in the areas surrounded by the hydraulic cast composed of cerebrospinal fluid.

of profound significance, and these shifts in volume ratio cannot be detected usually by spinal pressure determinations alone. The procedure of dehydration directed toward the removal of the excess volume of spinal fluid so as to permit replacement by an increase in circulating blood, offers a means of treatment in the acute as well as in the chronic mentally deteriorated groups.

The work of Whitney and Hunsicker [4] will clearly illustrate the futility of attempting a program on those cases where cooperation and reliability are lacking, and the possible advantage of these observations when considered in the light of the treatment lies in the direction of the prevention of chronic intracranial pressure disturbances by methods which will subtract the excessive cerebrospinal fluid volume from the craniovertebral cavity. When liquid intake has been strictly limited to 20 ounces per day, and the patient placed on a dry diet (Table III), with the necessary restrictions of salt and sweets, to prevent the tendencies toward water storage, pointed out by Gamble,[8, 8a] and with the distinct effort on the part of the clinician to reduce the patient's tissue water weight, there has followed a distinct improvement in mental activity.

The objections to the theory and formerly published results have been discussed in part II. and the fundamental basis for the concept of dehydration remains unchanged, in my opinion, when properly conducted.

SUMMARY.

Various groups of acute and subacute cerebral problems associated with mental deterioration have been presented, and the method of management indicated, which has been associated with arresting of the mental deterioration or with actual improvement in many cases where effectual cooperation and demonstrable dehydration have been accomplished.

That the results may indicate a possible line of approach in the more chronic type is suggested, as well as the need for preventive measures instituted along the lines of disturbed fluid metabolism of the body. This requires careful consideration in the management of such problems before profound states of deterioration have occurred.

TABLE III.

Diet Form and Instructions Used in Maintaining Dehydration.

Total allotment of fluid per 24 hours (tea, coffee, milk, water, soup, fruit juices, etc.) and total allotment of sugar per 24 hours.

Diet should consist of red and white meats, eggs, fresh water fish, dry cereals and the vegetables listed below in any variety, as well as butter, cheese, nuts, etc.

Portions of food should be moderate.
Meals of equal importance.
Avoid overeating at any time.
Avoid eating between meals.
One uncooked vegetable (carrot, lettuce, celery) *and* one fresh fruit (apple, orange, ½ grapefruit, pear, few grapes, etc.) allowed daily. Where juicy fruits or vegetables high in water content are desired, exchange for appropriate amount of fluid can be made by *cutting* total liquid intake allotted for the necessary amount substituted by the fruit or vegetable.

Vegetables Recommended.

Potato (baked, fried, French).
Peas.
Beans, navy and lima.
Carrots, Beets, Parsnips. } Drained of juice and served dry as possible.
Rice (dry steamed).
Corn.

For Thirst.

Warm Listerine gargle. For water may be substituted orange juice, grapefruit juice, White Rock, buttermilk, milk, tea, coffee, clear unseasoned soup.

Allotment of Liquids.

Breakfast .....ozs.
Breakfast to lunch.....ozs.
Lunch .....ozs.
Between lunch and dinner.....ozs.
Dinner .....ozs.
After dinner .....ozs.

Suggested Diet Proportions.

Breakfast: dry cereal (shredded wheat, corn flakes, puffed rice or wheat, etc.) with *measured* amount of milk or cream. Buttered toast, egg, measured amount of coffee.

Lunch: 1 potato, 1 other vegetable such as listed above. Red meat, fowl, cheese or fish (unsalted). Bread and butter, custard or junket.

Dinner: 2 vegetables from above, meat or eggs. Measured allotment of tea or coffee, milk or unseasoned soup. Fresh apple, salad or celery. No desserts. Fluids as above.

Vegetables to be Avoided or Exchanged for Liquid.

Asparagus.	Cauliflower.
Tomatoes.	Onions.
String beans.	Spinach.
Squash.	All greens.
Turnips.	Sweet potatoes.
Cabbage.	

Avoid Soggy Dishes.

Stews, puddings, macaroni, gravy, apple sauce.
No creamed preparations.

Avoid Fruits Such As

Melons, Peaches, Plums, Strawberries, Cherries. } These may be exchanged for a proportionate amount of allotted liquids.

Restrictions.

No Salt Added to Food.

No salty foods such as fish, chipped beef, saltines, pretzels, olives, salted nuts, etc.

No Sweets.

No ice cream, syrup, honey, jelly, cake, candy, canned fruits with syrup sauce. No sweet puddings, desserts or pie.

Desserts (Choice of 1).

Unfrosted cake, moderate portion.
1 cup custard.
1 junket.
Cookies (without icing or sugar).
Jello.
No sweet puddings, icings, pie, etc.

Weight Daily.

"A pint is a pound." Gain or loss in fluid can be checked by this means.

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DISCUSSION.

Dr. George Van Ness Dearborn (New York City).—Mr. President, certainly the research of Professor Fay and his colleagues is important and extremely interesting, and applies beautifully to a small group of the etiologies of acquired mental imperfection. But in the interests of scientific advance and accuracy, and that this paper's title may not be generally misleading, I think it is expedient to remind ourselves, as Professor Fay must know perfectly well, that the term "mental deficiency" is used throughout the English-speaking world for congenital mental defect, not for dementia and mental deterioration. I can't help feeling that to the large majority of people who pick up this paper in the future, the title will be directly misleading. There is mental deterioration of several types, notably, of course, affective deterioration and intellectual deterioration. As politely as the scientific circumstances allow, therefore, I suggest that this, properly speaking, is not a discussion primarily of "mental deficiency." The neuropathology of the other is now generally recognized to be somewhat different from that of mental defect, dementia, particularly in its complexity, and sometimes in its transitoriness. The paper is very instructive.

Dr. S. Bernard Wortis (New York City).—Whether one calls these cases mental deficiency or dementia should not prevent us from using the therapy Dr. Fay has outlined. It is not unusual to find brain tumors in patients in mental hospitals. Undoubtedly more meticulous neurological examination in suspected cases, with occasional brain exploration (when indicated) should be more often practised.

Dr. Alfred Gordon (Philadelphia, Pa.).—Mr. President, placing aside the problem of deterioration, I wish to speak particularly of the last case that Dr. Fay presented, namely the one with puncture of the lateral ventricles. May I ask you how many times you did that, Doctor?

DR. FAY.—I didn't puncture the ventricles in the last case—it was spinal drainage—drainage of fluid from the subarachnoid cortex.

DR. GORDON.—I had several cases in the last three years, I think four cases, of children presenting more or less pronounced hydrocephalus with the fontanelles widely dilated. In my judgment, all such children do not present mental deficiency, but, mental arrest or lack of complete mental development. The last of my series was extremely dull and had convulsive seizures almost every 10 or 15 minutes while it was being examined. The mother was desperate as to relief. Medication was given in different places, the regular standardized sedatives and restriction of diet, restriction of fluids, but the convulsions continued.

What I did, and what I keep on doing with these cases, was puncture of the lateral ventricles. I puncture one ventricle first and draw as much fluid as I can. The result is really remarkable. I dare not say the convulsions entirely disappear, that they don't come back, but the diminution was so striking that I cannot forget it. I have it constantly before my eyes. Mental development assumed its normal course. The patient was wide awake, played with toys, tried to grab things, where formerly it was entirely indifferent, had tremendous salivation, had dull appearance with the head hanging down. This improvement persisted for about six weeks, then it relapsed. We had a second lateral ventricle puncture and again I withdrew as much fluid as possible. Again there was a remarkable improvement. The child had all together not more than six ventricular punctures and we got results. The children are better physically and mentally. The last case is improving, but whether it will be maintained, I do not know yet. At any rate, what I want to put on record is the value of puncture of the lateral ventricles. I published two little articles in the *American Medical Association Journal* in which I said I have obtained satisfactory results without any medication.

I want to say just a word with regard to mental deficiency. I agree fully with the Doctor who said mental deficiency is somewhat misleading. I would say arrested mental development, insufficient development. Mental deficiency, as far as I am personally concerned, implies an entirely different state, a congenital condition, whether it is due to morphological changes of the brain or to hereditary elements that enter into it. Mental deficiency means a fundamental basal defect with an impossibility to improve.

DR. TEMPLE FAY (Philadelphia, Pa.) (in closing).—I wish to apologize to the Association if I have misused a term in this title but it required a great deal of thought to decide what to actually designate a group, an infantile group, if you like, which had no mentality to begin with and apparently lost very little. If we are to see this group later on, they will be classified as mental deficients certainly. If we see a progressive deterioration occur, as I pointed out in the acute cases—and the paper clearly distinguishes deterioration from deficiency—and if we did not know their former mentality and saw these patients for the first time, we should assume them to be mentally defec-

tive. The title perhaps is unfortunate, but it seems to indicate that these patients eventually are mentally defective, and whether we know the etiology of the so-called hereditary types, which I am sure as organic neurology goes on we are going to see more reasons for, it raises the question as to whether you can call it mental deficiency, deterioration, mental arrest, agenesis, abiotrophy or what not. The question arises if we are to assume the term as being confined to those groups. I would be glad to change the title of this paper because I feel that our terms are too loose and we cannot say that this is mental deficiency at eight months of age and this is mental deterioration at eight years of age. Certainly both of them have deteriorated from a certain point. If the child arrives in this world without any possibility of development, it is perhaps defective from the start. But I am sure that these processes occur acutely in both prenatal and postnatal periods, and that we do get deficiency in perhaps a similar way, and the etiology of which is to be determined.

Ventricular puncture *per se* is only a means which may perhaps stave off an acute cerebral compression. I wish to emphasize in closing that the only thing we have obtained in these cases or in any of the other cases is a better blood supply to the brain, better oxygenation and, therefore, better function and better retained function. I am sure that any process which attempts to keep intact that cerebral circulation and keep intact an adequate oxygen supply may save many brain cells during acute processes and may even prevent the very rapid deterioration that we see in the low-grade chronic processes which I believe are secondary to some form of cerebral anemia.

CONVULSIVE DISORDERS OF TWO OPPOSITE PERIODS OF LIFE: PUBERTY AND CLIMACTERIUM.*

By ALFRED GORDON, M. D., Philadelphia, Pa.

Continued experience with epileptic individuals teaches that until a definite pathogenetic element is established, one will have to depend upon speculative deductions from anatomical, physiological, pathological, biochemical, and psychological observations. It is evident that under such circumstances and in such a state of knowledge of the subject one is legitimately obliged to rely on all kinds of phenomena, normal or morbid, which even in the remotest way may assist in the elucidation of such a baffling problem as that of epilepsy. Among many observations in this direction, attention is presently drawn towards a possible relation of the disease to two physiological functions, namely, initiation of the menstrual periods and their cessation. Every observer has on his record cases in which convulsive disorders set in at puberty coincident with the phase of first ovulation and continue to occur each month about the same time, or else only occasionally but close to the date of the next menstruation. We are also aware of the fact that preexisting convulsive seizures may become decidedly aggravated at each menstrual period. One is equally familiar with cases in which convulsive disorders cease entirely with the progressive development of the climacteric period. Finally in some cases convulsions make their first appearance during the involutional period of life in women as well as in men. Is the chronological relationship between the genital life and convulsive seizures a mere coincidence or is it fundamentally physiological? So many observations came to our attention during a number of years that the idea of mere incidental coincidence must be discarded. In those cases the relationship was so close in time, in onset, in the clinical manifestations, that attention was strongly arrested on those phenomena and some explana-

*Read at the eighty-eighth annual meeting of The American Psychiatric Association, Section on Convulsive Disorders, Phila., Pa., May 30, 1932.

tion of the simultaneity of both disorders begged to be found. The following few examples present the problem in a striking light.

A woman of 39 commenced her epileptic attacks at the age of 13, the date of her first menstruation. Since then the convulsive seizures occurred each month, a few days before the first appearance of the flow and continued during the several days of the menstrual periods. She was free from attacks in the intervals. She is still menstruating at 39 and at no time has there been a diminution in intensity and duration of the attacks whenever medication would be discontinued either for the purpose of a test or because of a gastro-intestinal upset.

Another woman of 45 also commenced her epileptic seizures at the age of puberty and had them with great regularity in spite of medication during the periods of menstruation. At 21 she got married and in the following year she became pregnant. Her attacks ceased entirely during the nine months while no medication was being administered and during the following seven months while she nursed her child. With cessation of the lactation period the seizures reappeared.

The following case presents another peculiarity in the apparent reciprocal influence of the physiological process of menstruation and epileptic convulsions. An unmarried woman had seizures coinciding with the date of menses from the puberty-period up to the age of 42 when menopause commenced to develop with a series of distressing sympathetic phenomena, namely, flushes of heat, cardiac palpitation, restlessness and a minimum of menstrual flow. The attacks continued, being accompanied by the above symptoms up to the age of 45, when complete cessation of menses occurred. Since then there have been no attacks in spite of the discontinuance of sedatives.

Another example of a striking character came under the writer's notice three years ago. It concerns a single woman of 37, who, after a few days of malaise with a slight elevation of temperature, failed to observe her menses when they were actually due. They never returned since then. One week after that incidence a convulsive seizure occurred. During the three years of observation she had a large number of major attacks. I hasten to add that the latter were typical of epilepsy in all details.

In the presence of such striking occurrences the inference forces

itself upon the observer that some influence of the function of the female generative organs on the mechanism of convulsive seizures must exist. In this particular respect the few cases described must have a real value from the standpoint of pathogenesis of epilepsy. At this juncture it may be of interest to relate the history of a 29-year-old woman, who had epileptic seizures during her menstrual period. She accidentally fell and struck her abdomen against an iron bar. There was considerable vaginal bleeding at the time. For many months she complained of abdominal pain. A gynecologist advised a total hysterectomy. The uterus and ovaries were removed. Following this operative menopause the epileptic seizures have totally disappeared.

The few cases just reported are of course not unique. Literature contains many similar examples. If puberty and menstrual periods, if pregnancy, climacterium, castration—are all, at least in chronological relationship to the development or to disappearance of convulsive seizures, one cannot avoid reflecting upon a possible or probable reciprocal influence of one upon another in a physiological sense. On the other hand, there are many cases in which neither puberty, nor climacterium, nor menses, nor pregnancy, nor menopause are ever accompanied by convulsive seizures. There are also cases in which neither of these physiological processes has any favorable or unfavorable effect on the course of preexisting epileptic attacks. Scientific curiosity arises when one is confronted with such diametrically opposite observations. "In presence of uncertainties," said Claude Bernard, "the way of arriving at the truth is not to reject the positive facts in behalf of the negative ones and vice versa, but try to find the reason of their divergence."

The synchronism of the new puberty life and epilepsy in the first of these two opposing groups leads logically to the idea of a causal relationship. Let us consider briefly the modern view concerning the mechanism of normal menstruation and menopause. The menstrual cycle is controlled by the anterior lobe of the hypophysis. The latter secretes a hormone which stimulated the ovary. Under the influence of this stimulation the ovarian follicle increases in volume. The ovule contained in the follicle grows, the follicular cells proliferate and a certain number of the latter become liquefied. This fluid constitutes the internal secretion of the ovary. When the follicle is mature its theca breaks and the ovule falls in the tubes. The follicle is then transformed into corpus luteum. The theca,

follicular cells, the corpus luteum and placenta are the sources of the female sex hormone. Each month new follicles are formed under the influence of the antepituitary hormone. This notion is a recent acquisition and many clinical, experimental and therapeutic observations corroborate the relationship between the endocrinic secretion of the hypophysis and menstrual flow and its cessation at menopause. There are some substantial reasons to believe that the blood and other humoral substances of the body contain before the menstrual periods toxic substances which are the cause of the malaise experienced by the majority of women during the premenstrual period. It usually disappears during the flow. In cases of ovariectomies the malaise, which usually follows, disappears when ovarian grafts bring back the flow. It seems therefore that the menstrual flow relieves the body of toxic substances. The endocrinic secretion of the ovarian follicles plays a certain rôle in the general metabolism. Should it for any reason at all become disturbed, the metabolism will be disturbed. Besides, we are in possession of physiological and pathological facts indicating the influence of a disturbed secretion of one endocrinic gland upon that of other similar glands, all resulting in a profound disorder in the chemistry of the organism which means introduction in the blood and in all humoral substances of noxious material. For example, a disorder in the hypophysis disturbs the normal follicular secretion of the ovaries and at the same time the equilibrium in the function of the thyroid and the parathyroid bodies. Abnormal proteins or hormones from the latter are then discharged into the general circulation and produce an excitation of the psychomotor centers. This contention was proven experimentally on animals. That parathyroid insufficiently produces a convulsive poison in the economy is a classical notion at present. What particular poison elaborated by all these endocrinic glands is the direct convulsive agent, one cannot tell as yet. Increase of urea, increase or decrease of calcium, of creatine, of cholesterin, of sugar, etc., have all been incriminated. All we may say in the light of our present knowledge is that there must be a break in the mechanism which regulates the chemical equilibrium in some individuals during the menstrual period, during gestation, and with the onset of the climacterium. This break is produced primarily by the hormone of the anterior lobe of the hypophysis and secondarily by the influence of the

latter on other endocrinic glands. Through the concerted action of various ductless glands the humoral substances of the organism receive a convulsive chemical agent or agents which are an excitant to the psychomotor centers of the brain and produce epileptiform seizures.

The question now arises: are these chemical agents sufficient to produce convulsive seizures? There is one classical experiment among others which renders some assistance in solving this problem: while a dose of strychnia brought on epileptic attacks in dogs having had a cerebral lesion, the same dose failed to produce an identical clinical picture in animals whose brain was not previously damaged. It demonstrates therefore, the fact that old or recent cerebral lesions due to sequelæ of a former meningitis or meningo-encephalitis play an important rôle in the pathogenesis of epileptic seizures under all conditions. The late Jacob together with others called attention to developmental histological anomalies in many such cases. Asymmetry of the lateral ventricles, unilateral atrophic changes of one hemisphere or unilateral hydrocephaly—all are witnesses of old organic lesions. They may have been due to former toxi-infectious processes or to traumatism of old standing. In all such cases there are modifications of the nerve cells which render them highly sensitive to irritating agents which may come from any source.

The above considerations concerning the part played by endocrinic glands in relation to epilepsy and the few examples among many others referable to the association of epilepsy with the onset of puberty, with cessation of menstrual periods, and with pregnancy; finally the value of an old cerebral lesion in the analysis of epilepsy—all these facts lead one to the necessity of associating a lesional factor and a humoral agent. Clinical, anatomo-pathological and experimental researches lead to this inevitable conclusion. Experimental method alone demonstrated the fact that direct stimulation of nerve centers, whether it is electrical, traumatic or chemical, determines convulsive seizures apparently as a result of chemical and physical alteration of the nerve-cells. As far as the humoral chemical agent is concerned, there may be not only one but many (see above). It is impossible as yet to say whether the latter act directly on the nerve-cells or through the vagosympathetic system, which produces a local vasomotor disorder in the cerebrum (vaso-

dilation or vasoconstriction—hyperemia or ischemia). A vago-sympathetic disturbance may carry its effect not only on the blood-vessels but also on the choroid plexuses and produce an excessive secretion within the ventricles with the result of intracranial hypertension and therefore convulsive seizures.

So far we have been able to incriminate in epilepsy a lesional state of nerve-cells in the psychomotor center of the cerebrum, a vasomotor disorder at the same level produced by agents of a chemical nature elaborated by the anterior portion of the hypophysis in association with other endocrinic glands and finally, the vago-sympathetic system.

As to the influence of the hypophysis, we are in possession of a mass of evidence. The relationship of this gland to the infundibulum and tuber cinereum is a very close one. Experimental injections of potassium chlorate into the infundibulum produced convulsions (Demole. Arch. f. exper. med., 1927). The same result was obtained when the injection was made in the walls of the third ventricle. The same was observed from injections of silver nitrate into the tuber cinereum (Morgan. Arch. of Neur. and Psych., 1930). Sudden hypertension of the third ventricle is apt to bring on attacks of convulsive seizures (Greving. Klin. Wch., 1928). All these anatomical elements, namely, infundibulum, tuber cinereum, third ventricle, and the hypophysis, belong to the same portion of the brain, namely, the diencephalon. Alterations in any of its constituents lead to convulsive seizures; but clinical, anatomopathological and experimental data tend to prove that the hypophysis suffers in lesions of any other part of the diencephalon. Tumors, hemorrhages, atrophy, or hypertrophy, abscess of the hypophysis, have all been accompanied by convulsive disorders. Lowenstein observed in 30 out of 100 epileptics hypophyseal characteristics, namely, acromegalic facies, adiposogenital syndrome, polyuria, and changes in the sella turcica, and he obtained favorable results in treating the convulsive seizures with pituitary extracts (Amer. J. of Med. Sc., 1922). Hypophyseal opotherapy in convulsions gave also favorable results to Kiyone and Budde (Virch. Arc., 1926) and to Frazier (Trans. Am. Neur. Assn., 1928). Irradiation of the hypophysis in epilepsy was also successful in the hands of Buscaine (Rass. clin. scientifica, No. 12, 1928). Houssay and Giusti observed experimentally that convulsive seizures, which

appeared after hypophysectomy, disappeared when a hypophyseal grafting was performed (C. R. Sec. de Biologie. Aôut., 1922). Altenburger and Stern are convinced from their studies that insufficiency of the pituitary function constitutes one of the fundamental pathogenic conditions of epilepsy (Zentralbl. f. d. ges. Neur. u. Psych., 1929).

On the first pages mention was made of suspension of epileptic seizures in some cases during pregnancy. Ascheim and Zondek have shown that in pregnancy there is a considerable increase of hormones from the anterior lobe of the hypophysis in the urine and blood. Thyroidectomy and adrenalectomy have been followed by a diminution of convulsive seizures because of hyperfunction of the hypophysis. On the other hand, cases have been observed in which convulsive seizures made their first appearance during pregnancy or after ovariectomy. In such cases the hypophysis was found to be pathological. Imperato speaks of an increased toxicity of the hypophysis in puerperal eclampsia (Arch. di Ostetricia, e Ginecologia, 1929). All these data tend to prove the fact that the close functional relationship between the hypophysis and the generative glands, the thyroid, adrenals, etc., explain the convulsive seizures observed in cases in which physiological and pathological alterations of these glands occur, as for example, at the two opposed periods of life, namely, puberty and climacteric period. The hypophysis, one of the components of the diencephalon, is in close relation to the infundibulum and the tuber cinereum which are the other two portions of the diencephalon and which, as mentioned above, if stimulated, also produce convulsive disorders. Stimulation of one or of all these anatomical elements is followed by a hypersecretion of pituitrin which possesses convulsive properties, either directly through its toxic characteristics or through a considerable increase of the cerebrospinal tension.

The object of this essay is to consider one of many phases in the history of pathogenesis of epilepsy. While the clinical, histological, chemical and experimental efforts to determine a definite causative factor for this enigmatic disease have not been altogether successful, nevertheless an analytical approach to the problem based on modern scientific data helps to ameliorate the situation in some cases. The discovery of the influence of the anterior lobe of the pituitary upon the follicular function of the ovary on the one hand,

and its effect on convulsive disorders on the other, is one of such examples. The therapeutic efficacy of the follicular hormone establishes a firm relationship between epilepsy and the great crises of genital life at the two opposite poles of the latter in a certain group of cases.

In the discussion of the pathogenesis, exclusive attention was so far directed to the physiological, anatomical, and chemical levels of the problem. The subject cannot be complete if some consideration is not given to a still other important level, namely, psychological. With the advent of Freud's teaching which aims at the study of the total personality any scientific question in medicine cannot and should not be considered exhausted without an endeavor to determine a possible relationship of somatic phenomena to the psychological content of the affected personality. If we recall the histories of the few special cases described above, we find in some the onset of convulsive seizures only at the age of puberty, their occurrence only during menstrual periods, their cessation at the climacterium; we find some with cessation of attacks during pregnancy and recurrence after the period of lactation; there was one case of a young woman who after a vague attack of some infection ceased to menstruate but instead developed convulsive seizures; one case of another young woman suffering from epileptic seizures which disappeared totally after a hysterectomy. In initiation of menstrual periods, in their temporary or permanent arrest during pregnancies, in their resumption after the lactation period is over, in their complete disappearance after removal of the internal genitalia—in all such states we observed convulsive types of reaction conditioned by physiological situations. Although menses, pregnancy, lactation are physiological functions, nevertheless they are situations intolerable to some individuals when no adjustment was possible for them; they lost more or less consciousness, the normal and purposeful muscular reactions became disorganized, incoordinate movements as well as rigidity were the result. These phenomena appeared to be a retreat or a flight from reality and a way of finding pleasure by a deep regression. Ferenci very aptly calls it a wish-fulfilment (Internat. Ztschr. f. aertzt. Psychoanalyse, v. 1, 1913). This flight from reality by means of an unconscious state during a seizure and the manifestations observed during the

individual's attempt to return to reality with the gradual return to consciousness, are indications how the above mentioned intolerable situation led some individuals to seizures which served a certain purpose, namely, to escape from unavoidable physiological function necessitating some responsibility on their part and at the same time to avoid adjustment. An analysis of all the elements here involved demonstrates the fact that in order to understand the mechanism of epileptic attacks in some cases, such as those related above one must admit that in spite of the biological character and the inevitableness of the adjustment a conflict is created and the inability of a conscious adaptation leads to a state of unconsciousness and of muscular struggle in the form of convulsions. The toxicity of the hormonic origin discussed on the first pages may be the organic factor capable of exciting convulsive disorders at certain important periods of life in a certain group of individuals, but the *modus operandi* cannot be fully understood if besides the sensorimotor and a metabolic level the psychological setting is not taken into consideration. The only method of approach for a full understanding of problems in individual cases is an analysis of all phenomena, somatic as well as psychological.

DISCUSSION.

Dr. Robert L. Dixon (Lapeer, Mich.).—Mr. Chairman, the cases which Dr. Gordon has presented to us are quite prominent in all of our experiences. All of us have seen many epileptics whose seizures have an onset at the time of puberty or at the time of the menopause or some other essential period in life.

I think Dr. Gordon struck one very important point, which he did not emphasize quite as much as I wish he had, when he said that these periods were intolerable to certain people. There is the point exactly. Those certain people are the epileptic people. I quite firmly believe that all of those persons who had this initial convulsion at the time of puberty or at the time of menopause or under the other conditions which Dr. Gordon mentioned, should have been and could well have been diagnosed as epileptics prior to that time.

Dr. S. Bernard Wortis (New York City).—It is perhaps interesting, at this point, to mention that Adie many years ago described a type of epilepsy which he called pyknolepsy, which stops at the time of puberty. It seems unwise to postulate only one physiological derangement as the common causative factor of all types of convulsive seizures.

About two years ago, Dr. Morgan presented some experimental and pathological studies in which he felt that the tuber cinereum was "the" specific convulsogenic center. We have some evidence to present this afternoon which I think will question this conclusion. That is confirmed by much other evidence. There are a great many cases in the literature where pathological lesions exist in the tuber cinereum without convulsions and I refer particularly to the work of Fulton and Bailey who collected a large series of tumors of the third ventricle and the tuber cinereum; many of their cases did not have convulsions.

I think Dr. Gordon is quite right in emphasizing the psychological approach to certain cases of epilepsy.

Dr. Alfred Gordon (Philadelphia, Pa.) (in closing).—The doctor mentioned "certain people." That is perfectly true. Just as I mentioned in the paper very conservatively, not all individuals develop epilepsy at the period of puberty or the period of the climacterium. Certainly not; I emphasized the point. The doctor is inclined to call them epileptics even if they did not have epilepsy before those two periods of life. That is possible. I agree with him that there is a certain make-up of these individuals but who under the influence of intoxication or under the influence of a peculiar psychological make-up avoid adjustment for inevitable situations such as menstruation and unconsciously find an escape in their disturbance, of which they are not aware, such as epileptic convulsions.

What I particularly aimed at in addition to the pathogenetic feature of the subject is the possibility of the therapeutic approach. This is more important than anything else to these individuals. We have a hard time with individuals whose mothers come and ask us to prevent the oncoming menstruation, the next menstruation, in order to prevent an epileptic attack. In order to solve these difficult, perplexing problems which we cannot fully understand, it is valuable, as I said, in a number of instances to consider the subject from every possible angle, remove all possible toxicity, remove any possibility of metabolic disturbances at the chemical level; regulate the individual's behavior in such a way as to avoid undue emotional disturbances; prescribe the anterior lobe of the hypophysis, but particularly (and some may not agree) take special interest in the psychological attitude of the patient which can be successfully applied only when a complete longitudinal history is taken of the individual from childhood up, and size up his make-up, the hereditary factors, and his reaction to emotional disorders of any kind.

NARCOLEPSY.*

By S. BERNARD WORTIS, M. D., AND FOSTER KENNEDY, M. D.,
New York City.

Historical Review.

The symptomatology of narcolepsy was first described by Westphall [37] in 1877. Subsequently Gelineau [12] (1880) delineated a specific symptom-complex characterized by recurrent attacks of irresistible sleep at times associated, during periods of acute emotion, with loss of muscular power and tone causing the subject to fall powerless. Sir William Gowers [13] in 1907 and recently Worcester-Drought [39] and others have pointed out the relationship of this symptom-complex with that of epilepsy. The relatively infrequent occurrence of cases of narcolepsy 25 years ago has been attested by S. A. K. Wilson [36] in England, and Spiller [32] in this country More recent reports by Lowenfeld [22] (1902), Hennenberg [14] (1916), Redlich [25] (1915), Goldflam [11] (1924), Adie [1] (1926), Levine [20] (1929), Brock [5] (1928), Cave [6] (1931), Doyle and Daniels [9] (1931), Odell [23] (1932) and others are evidence to the greater frequency of occurrence and recognition of narcolepsy and its variations.

Adie [1] considers Gelineau's narcolepsy a disease *sui generis*. The present view of most clinicians seems to be, as Wilson stated, that "for present purposes, the narcolepsies stand for the hypersomnic varieties of sleep disorder, whatever their etiology, among which it is convenient to distinguish a combined type corresponding to that so well differentiated by Gelineau."

Etiology and Pathology.

Most authors including Lhermitte, Tourney,[21] Wilson [36] and Brock [5] have subdivided the narcolepsies into the following groups:

1. Traumatic. (Cases reported by Singer, Redlich, Wilson.)
2. Psychopathologic. (Cases reported by Worcester-Drought and Myers.)

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3. Toxic-infective (post encephalitic, post pneumonic, post scarlet fever). (Cases reported by most authors.)
4. Circulatory.
5. Pressure caused by neoplasm about third ventricle. (Cases reported by Soca, Fulton and Bailey *et al.*)
6. Endocrine. (Cases reported by Curschman, Wilson *et al.*)
7. Epileptic. (Cases reported by Gowers, Goldflam, Worcester-Drought and Zadore.)
8. "Idiopathic" variety. (All authors.)

The precise pathology causing narcoleptic seizures is not known, since to this date no one has published a histopathological study of a so-called "idiopathic case." The disease of itself is not fatal and statistical compilation of groups of reported cases indicates a greater incidence in males (approximately 6 to 1), usually beginning in the second decade and persisting for varying periods.

Lacking precise knowledge of the cause of this malady, theories become abundant. Gelineau regarded this syndrome as partaking of the nature of a neurosis. Hercouet [15] (1905), McKendree and Feiner [24] (1927), Lhermitte and Tourney [21] (1927) stress the fact that sleep alone has no certain cerebral localizing value but that it occurs more frequently in tumors at the base of the brain. Righetti [18] studied 775 cases of verified brain tumor, 115 of which had pathological sleep. Of these 115 cases 86 per cent presented tumors in the region of the thalamus and third ventricle, hypophysis and the corpora quadrigemina.

Moreover a few specific case reports are important in this regard. Baruk, Bertrand and Souques [2] reported a case of a woman suffering with headaches and extreme sleepiness of over six months' duration, who at necropsy was shown to have a small tumor in the region of the tuber cinereum pressing up into the floor of the third ventricle. Lucksch [25] (1924) and Pette [27] (1923) reported cases with abscesses and thrombotic embolic lesions in the region of the walls of the third ventricle, and about the nuclei of the third nerve, the aqueduct of Sylvius and proximate parts of the thalamus. C. von Economo,[9] in his excellent studies of epidemic encephalitis, was also able to associate sleep disturbances with lesions of this region of the brain. Alajouanne, Lagrange and Baruk (1925) reported a case of undoubted (but not proved) tumor of the pineal body, with associated seizures simulating narcolepsy. Recently Fulton and Bailey [10] have completed an excellent review of

this subject and believe, in part from the study of their group of tumors in this region, that disease of the floor of the third ventricle—iter region—causes "disturbances of normal sleep rhythm but not necessarily hypersomnia."

Pavlov [38] in his remarkable studies of conditioned reflexes concludes that "sleep and internal inhibition are essentially one and the same process." Painful repeated electric shock stimuli produced sleep in Pavlov's animals, provided no other dissimilar stimuli were allowed to reach the cortex. By this process Pavlov believes the receptive cortical area became fatigued (slept) and the inhibitory function spread to produce general sleep. This hypothesis is also held by Worrall [40] (1931) who concludes that "experimental and clinical evidence supports the view that unconsciousness is the result of a process of physiological inhibition extending over the whole of the cerebral cortex" and that many cases of narcolepsy are the resultants of such a process. Although, as S. A. K. Wilson has pointed out, this explanation aids us in understanding the cataplexy often associated with narcoleptic seizures, it does not entirely satisfy our comprehension of the sudden sleep and cataplectic seizures.

There is moreover another bit of evidence which favors the postulation of a focal functional lesion in this disease. The not infrequent relationship between hypersomnia, adiposity, genital dystrophy and polyuria is well known, from both experimental and clinical evidence, to be related to lesions in the hypothalamic or tuber cinereum region.

It would seem logical, therefore, to look upon narcolepsy as a symptom-complex denoting an underlying neurophysiological derangement probably of an organic (physico-chemical) nature in the region of the floor of the third ventricle and periaqueductal regions.

Clinical Manifestations and Variations.

One or more of the following cardinal symptoms occur in cases of true narcolepsy.

1. *Sleep or Trance-Like States.*—These most often come on suddenly without apparent cause in diverse circumstances. Such overpowering "sleep attacks" are usually precipitated by acute emotional states—most frequently laughter—and ordinarily cannot

be resisted by the patient. The attacks may be of a short transitory nature or may persist for several minutes or hours. Sleep seizures have been known to occur while the patients were actively at manual work, while driving an automobile, or while walking or talking. The "sleep" may be deep but most often is very light and the patient can usually be instantly aroused to acute awareness. Patients have been known to carry out automatic reflex activities—as walking or talking "jargon"—whilst having light trance-like seizures. Often the patient's facies simulates sleepiness because of associated cataplexy; however under such circumstances he is entirely aware of his environment and can later describe events that occurred during the attack.

2. *Attacks of Cataplexy.*—Sudden emotional stress results in sudden complete loss of skeletal muscular tone—so that the patient falls to the ground weak, powerless and helpless, though fully conscious. Reading of a happy event, or embracing a girl, or laughing at a funny story has been known to precipitate such seizures. Rarely extreme depression has precipitated cataplectic seizures. Patients being fully aware of such cataplectic humiliations try hard to avoid them by barricading themselves with an air of solemnity. Attacks of cataplexy are very brief—a few seconds or moments—and during them the pupillary and deep muscle tendon reflexes are not elicitable; while a positive Babinski sign can be obtained. The jaw, eyelids and the head may droop; there may be myoclonic twitchings of the facial muscles or the arms; and some cases with transient blurred vision have been reported. With the return of muscle tone and power these abnormal states vanish.

3. *Catalepsy.*—This refers to the state of immobility associated with full consciousness which obtains in many of these patients. They cannot so much as "wiggle a finger" to save themselves. Such predicaments are usually attendant upon cataplectic attacks. Richter [30] by studying the electrical skin resistance of patients in normal and pathological sleep-like states has shown that the skin resistance of people suffering with narcolepsy is higher than that of normal people, and implies that important psychomotor changes have taken place in these subjects.

Obesity, migrainous attacks, epilepsy and "hypnopompic hallucinations" occasionally coexist in these patients. These attacks of

narcolepsy with catalepsy must be differentiated from hysteria, "Lachschlag" of Oppenheim, epilepsy, pyknolepsy and attacks of "periodic family paralysis."

THERAPY.

During the past year we have had occasion to treat six patients suffering with narcolepsy. They gave no history of lues; all had negative blood serology. Complete neurological examination re-

REPORTED EFFECTS OF DIFFERENT TYPES OF THERAPY IN NARCOLEPSY.

Drug.	Reduced number of seizures.	No effect on seizures.
Caffeine	Birman (1928)	Redlich (1925). Hennenberg (1916).
Strychnine		Redlich (1925).
Phenolbarbital or bromides	+ caffeine, Hilpert (1925).	Adie (1926). Urlson (1928). Cave (1931). Most authors. Wilson (1928).
Rest in bed, no drugs	Hennenberg (1916). Cave (1931).	
Thyroid	Dercum (1913) Wenderovic (1924) Matzdorf (1925) Weech (1926).	Birman (1928). Pierce (1928). Ratner (1928).
Mixture of opium, strychnine, caffeine.	Bostock (1928).	
Pluriglandular medication	Janzen (1926) Ratner (1928) (pituitary subst.).	+ thyroid + caffeine. Brock (1926).
Lumbar puncture	Lhermitte and Nichols (1929).	
Psychotherapy	Lowenfeld (1902). Hypnosis: Myers (1920). Psychoanalysis: Missriegler (1924). Suggestion: Villaverde (1928).	
Ephedrine	Janota and Skala (1930). Doyle and Daniels (1931). Odell (1932). Cave (1931).	

vealed no aberrations suggestive of brain tumor. Skull X-rays, blood chemistry and urine examinations were normal. No history of significant head trauma was related to any of these cases. Two of the patients were obese and gave histories suggestive of having had encephalitic infections. It is needless here to report each patient's

story in punctilious detail, since this syndrome is now well recognized and no striking deviation from the usual picture was observed.

Review of the literature up to 1930 relative to therapy of this disease shows that most cases run a chronic course and occasionally improve spontaneously. Most observers agree that the common sedative drugs have no effect in relieving the occurrence of narcoleptic seizures.

Case.	Probable etiology.	Caffeine sodiobenzoate, Grs. II, T. I. D.	Ephedrine sulphate, Grs. ¾, T. I. D.	Thyroid, Grs. ½, T. I. D.
M. B.	"Idiopathic" ...	Not used in this case.	Stopped narcolepsy and cataplexy.	Stopped narcolepsy and cataplexy.
E.....	"Idiopathic" ...	No effect on narcolepsy or cataplexy.	Stopped cataplexy. No effect on narcolepsy even with ¾ grs. 4 times daily.	No effect on narcolepsy or cataplexy.
C. W.	"Idiopathic" ...	No effect on narcolepsy or cataplexy.	Stopped cataplexy. No effect on narcolepsy.	No effect on narcolepsy or cataplexy.
M. W.	"Idiopathic" ...	No effect on narcolepsy or cataplexy.	Diminished but did not stop narcolepsy. Helped but did not stop cataplexy.	No effect on narcolepsy or cataplexy.
J. J...	"Post-encephalitic" with obesity.	No effect on narcolepsy or cataplexy.	Stopped cataplexy. No effect on narcolepsy.	No effect on narcolepsy or cataplexy.
A. W..	"Post-encephalitic" with obesity.	Slight diminution in narcolepsy. This patient had no cataplectic fits.	No effect on narcolepsy.	Slight diminution in narcolepsy.

Arguing from the hypothesis that attacks of cataplexy were the result of insufficient suprarenal glandular activity in times of emotional stress Chen and Schmidt[7] (1926), J. L. Johnson (1931), Janota and Skala[25] (1930) and Doyle and Daniels[8] (1931) suggested the use of ephedrine sulphate medication. Also because of the fact that ephedrine counteracts the sodium amytal narcotic effect—and moreover of itself when given in large doses results in sleeplessness—Doyle and Daniels used ephedrine and reported complete relief in five of six patients. Odell (1932) reported six cases of which three treated with ephedrine were markedly improved. Five of our six patients had cataplexy, associated with narcolepsy; 4 were helped by the use of ephedrine sulphate in ¾ grain doses

three times daily. The sixth patient had no cataplectic seizures. In only two of the six cases was any benefit noted in relieving the sudden attacks of sleepiness. Two patients were improved of sleep seizures and one of these also of cataplexy, by thyroid gland medication. Caffeine sodiobenzoate was also tried on five of these subjects, but did not appear to be of value in diminishing the sleep attacks or preventing the cataplectic mishaps.

It would appear, therefore, from experience with this small group of subjects that ephedrine is of some value in the control of the cataplectic seizures in some cases of narcolepsy, and that it is less efficacious in stopping the attacks of sleep. Study of a larger group of these cases is necessary.

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DISCUSSION.

Dr. Howard D. McIntyre (Cincinnati, Ohio).—Mr. President, I have seen five cases of this condition reported by Dr. Wortis. Four of these patients were observed at the diagnostic center at the Cincinnati General Hospital. In all of them narcolepsy was a sequela of lethargic encephalitis. One of these patients was employed as a garage mechanic. He would go to sleep under a car that was jacked up above him and would go to sleep in other positions exposing him to great danger. He would go to sleep driving an automobile and had quite a number of accidents for that reason.

One of the patients gives a history similar to a case reported by Dr. Spiller of Philadelphia. This patient liked very much to fish and he was in the habit of fishing in a canoe. He would go to sleep in the canoe and it would turn over and he would fall out into the cold water. The cold water would waken him and he would climb back into the canoe and resume his fishing.

All four of these cases gave a definite history of lethargic encephalitis. Two of them showed mild extrapyramidal syndromes. The fifth case was probably on an endocrine basis. This patient was a college student, age 22. He was failing in his classes because he was unable to keep awake during class. This patient had a basal metabolic rate of minus 50%, one of the lowest I have recorded. It was very interesting to note that low basal metabolic rates are the rule in most cases of narcolepsy. In three of my patients the rate varied from minus 20% to minus 50%.

As to treatment I used thyroid extract with excellent results. This was before the papers dealing with ephedrine as a therapeutic agent had been published.

My fifth case, the college student who was unable to keep awake in class, did particularly well on ephedrine.

Dr. S. Bernard Wortis (New York City) (in closing).—I want to thank Dr. McIntyre. It is most important that we gather groups of these cases, though they be small groups, in an attempt to determine the best type of therapy. I believe we shall find that there is no reason for assuming that any one type of therapy can help all cases of narcolepsy, just as we know that one therapy cannot mitigate all causes of epilepsy. The low basal metabolic rate is not found uniformly, although it is occasionally seen in cases with metabolic aberrations secondary to postencephalitic infection.

THE EFFECTS OF THE SAME DRUG, OR OTHER EXPERIMENTAL PROCEDURE, UPON CONVULSIONS ELICITED IN ANIMALS BY DIFFERENT EXPERIMENTAL METHODS.*

By F. H. PIKE, Ph. D., J. NOTKIN, M. D., HELEN C. COOMBS, Ph.D. and S. M WEINGROW, M. D.

General Statement.
The Problems of Localization and of Pathogenesis.
The Methods of Inducing Convulsions Experimentally.
The Quantitative Estimation of the Dosage of Absinth.
The Experimental Results.
The Effects of the Injection of Hypertonic, Isotonic and Hypotonic Fluids upon Convulsions Induced by Absinth.
The Effects of Hæmorrhage and of the Injection of Isotonic Fluids upon Convulsions Induced by Absinth.
The Effects of Variations in Intracranial Pressure upon Convulsions Induced by Absinth.
The Effects of the Injection of Hypertonic and Hypotonic Fluids upon the Reaction to Cerebral Anæmia.
The Effects of the Injection of Hypertonic Fluids upon the Reaction to Electrical Excitation of the Cerebral Cortex.
The Effects of the Injection of Hypotonic Fluids upon the Reaction to Electrical Excitation of the Cerebral Cortex.
The Bromides.
The Effects of Bromides upon Convulsions Induced by Absinth.
The Combined Effects of the Administration of Bromides and the Injection of Hypertonic Glucose upon Convulsions Induced by Absinth.
The Effects of the Administration of Bromides upon the Reaction to Cerebral Anæmia.
The Effects of the Administration of Bromides upon the Reaction to Electrical Excitation of the Cerebral Cortex.

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The experiments in which measurements of blood-pressure were made, or the cerebral arteries ligated, were done in the laboratory of physiology, at the New York Homeopathic Medical College. All other experiments were done in the laboratories of Columbia University.

The Effects of Trional.
The Effects of Trional upon Convulsions Induced by Absinth.
The Effects of Trional upon the Reaction to Cerebral Anæmia.
The Effects of Trional upon the Reaction to Electrical Excitation of the Cerebral Cortex.
General Comment.
Tabular Summary.

General Statement.

The experimental study of the convulsive states, so far as it concerns epilepsy alone, the results of which now constitute a great volume of literature, has been based very largely upon relatively few general principles or upon a relatively small number of hypotheses of the nature of the convulsive states. The problem of the convulsive states is considerably wider than that of the problem of epilepsy. To quote the opinion of a general pathologist: "Tetany and convulsions are not due to any single cause. Any one of a multitude of disturbances in the equilibrium within certain tissues may be responsible. Convulsions are to be regarded as a sign of approaching or partial disintegration of the neuromuscular apparatus. The defect may occur in any one of several structures and may be due to any one of many causes." (MacCallum, *et al.*) In the narrower province of epilepsy, we may divide the field of investigation into two principal domains, namely (1) the domain of the search for the region or regions of the nervous system from which the motor impulses responsible for the visible manifestations of the convulsion arise, and (2) that of the search for the actual agent which acts upon the motor cells of the central nervous system in such a way as to give rise to those motor phenomena.

The Problems of Localization and Pathogenesis.

The first domain is that of localization, and practically every region of the central nervous system has been included within it by one writer or another. The first attempt to put this part of the inquiry upon a definite anatomical basis was that of Hughlings Jackson, who thought that convulsions, particularly those of Jacksonian epilepsy, were due to some effect upon cells in the cerebral cortex. It will be recalled that, subsequently to his localization in the cerebral cortex of the cells of origin of the nervous impulses leading to the motor manifestation of convulsions, Jackson was led

to postulate a theory of the evolution of the human nervous system, and a further theory of the functional relation and organization of its various divisions in order to understand the varied phenomena of convulsions. We have available to-day more facts drawn from a wider field of general biology than were available in Jackson's day, but the necessity of considering the problem of the convulsive disorders from the point of view of the functional organization and evolution of the nervous system is as pressing to-day as it was then.

Jackson broke sharply with tradition when he abandoned Kussmaul and Tenner's views that convulsions arose from a "*Krampfzentrum*" in the medulla oblongata. The great viability of the hypothesis of "convulsive centers" in various regions of the nervous system makes it permissible to call attention to some of the conditions which such hypotheses must meet. It will be remembered that, in Jackson's own time, the objection was raised that unless the convulsion arose from the "*Krampfzentrum*" in the medulla, it could not be considered true epilepsy.

Any "convulsive center" in the medulla could act directly only upon the cells of origin of efferent fibers in the medulla itself, and not upon cells of origin of fibers from any other region. It is doubtful whether the cells in the reticular formation give rise to a sufficient number of fibers to produce all the somatic and visceral responses of a typical convulsion in man or the higher mammals, and no clonic convulsion is obtainable in higher mammals when all structures cephalad to the medulla are removed. If disturbances arising in the medulla are supposed to excite the fibers arising from cells higher up, one wonders just how such a center can act upon fibers with which it has no direct connection.

A similar argument could be adduced with reference to some other regions of the nervous system which have been held to be the site of origin of epileptic convulsions, and particularly those regions in which dead cells are found. No one has ever succeeded in getting a nervous impulse from a dead cell, and it is to the cells that are still alive that we must look for the origin of the nervous impulses which give rise to the motor phenomena of convulsions. The problems of localization and other aspects of epilepsy have recently been reviewed by Krause and Schum, and we will not follow them further at this time.

The second domain is that of the pathogenesis or cause of the convulsions. Here again, practically every condition which arises within the animal organism has been held responsible. It is not so long ago, that, judging by the names applied, some forms of epilepsy were held to be their own cause, as, for example, so-called idiopathic epilepsy. If the word idiopathic signifies anything, it means that idiopathic epilepsy is its own cause, and hence, that this cause cannot be discovered by varying the conditions under which the convulsions occur. A more hopeful view is that no form of epilepsy is really idiopathic, and that its cause may eventually be discovered. The possibility of an attempt at the explanation of the origin of convulsions in terms of physics and chemistry first became apparent when Haller's idea of a *vis nervosa* began to supplant Stahl's conception of an *anima sensitiva* in the minds of physiologists in the eighteenth century. As working hypotheses, we have the views that (1) convulsions are due to some chemical change somewhere within the organism, such as a circulating toxin; (2) that they are due to some physical agent, such as an anatomical change or a new growth within the central system; and (3) that the chain of events leading up to a convulsive manifestation may involve both physical and chemical agents, such as some physical or chemical agent acting upon the vascular system and inducing a convulsion through the chemical changes in the nerve cell following upon the interference with its blood supply. Anaphylactic and sensitization phenomena might be included here or under the first heading. We may recall that Jackson insisted upon some diseased condition of the middle cerebral artery as an accompanying condition in cases of Jacksonian and general epilepsy. Cobb has recently presented a longer statement of the views on the pathogenesis of convulsions.

THE METHODS OF INDUCING CONVULSIONS EXPERIMENTALLY.

Consonant with these various hypotheses of the nature of the cause of epilepsy, the methods of inducing convulsions experimentally may be grouped as:

1. The introduction of some toxic substance into the circulation directly or indirectly, or into the nervous system itself. The intravenous injection of absinth or camphor monobromide or their administration by mouth or stomach tube may be taken as an

example of this method. The first use of absinth for this purpose dates back to Marcè and Magnan.

2. The induction of changes in the vascular conditions in the central nervous system by direct ligation or blocking, temporary or permanent, of cerebral arteries or veins may be taken as an example of the method of inducing convulsions by changes in the blood supply of the central nerve cells.

3. Electrical excitation of the cerebral cortex, particularly of the motor areas, may be taken as an example of the method of experimental induction of convulsions by a physical agent.

Each method has its own peculiar advantages and yields its own peculiar results from the point of view of the nature of the processes set up in the nerve cells.

The method of intravenous injection of absinth has the advantage of ease of administration, since no previous operative procedure, except the trivial one of exposure of the internal saphenous vein, under local anæsthesia, is necessary as it would be if one were to expose the cerebral cortex or cerebral blood-vessels, so that the time necessary for preparation for an experiment is measurably reduced. It also possesses the advantage of more accurate quantitative estimation than is now possible with other methods. It is the method which we have employed most extensively. It has the disadvantage of employing a toxic substance and of producing its effect by chemical excitation only; and chemical excitation may differ in its effects upon nerve-cells and in its mechanism from the mechanism and the effects upon the cell of other methods of excitation. If any parallelism exists between the action of absinth upon nerve-cells and the action of some other chemical substances upon other cells, as for example, the action of the alkaloid muscarin upon the heart of the invertebrate Aplysia (Straub), it can act only when the concentration of absinth outside the nerve-cell is greater than its concentration within the cell. This is one consequence of DuBois-Reymond's law of stimulation—that the excitatory effect does not seem to be so much a function of the intensity alone, as of the rate of change of the intensity, that is, of $\frac{dI}{dT}$, where I is the intensity and T the time (Gotch).

The method of inducing convulsions by interference with the cerebral blood supply has been known so long that its origin is

apparently lost in the mists of antiquity. In more recent times, it was apparently used by Stensen, although he did not tie off the arteries to the head, in the sixteenth century and by various subsequent workers. This method was brought to a high degree of development by Leonard Hill at the opening of the present century. It has the advantage of adding no extraneous chemical substance, either to the nervous system or to the system in general, and of not requiring any direct exposure of any portion of the central nervous system. It has the disadvantages of requiring the prior use of an anæsthetic and of not being amenable to quantitative measurement. Furthermore, the apparent hyperexcitability of the central nervous system observed during the early stages of the cerebral anæmia reappears in reverse order with the recovery of the central nervous system consequent to reëstablishment of the cerebral circulation. This hyperexcitability occurring during the stage of failure of function, and during the stage of return of function, may be demonstrated in peripheral nerve fibers also. It comes out in a particularly striking way in the reaction of the left phrenic nerve to the action current of the heart (Pike). The literature on the subject is extensive (Winkin).

The effect of reduction or total stoppage of the blood supply to any organ or tissue is probably not due solely to the relative absence of blood, but to the lack of oxygen and the accumulation of carbon dioxide and other end products of metabolism of the tissues as well. Anoxæmia alone, in so far as it signifies absence of oxygen without an increase in the concentration of carbon dioxide, would not be a strict equivalent of ischæmia or anæmia. A parallel case, on the basis of the law of mass action, would be the failure of fermentation by yeast from the absence of sugar alone, as compared to the slowing down of the process from the accumulation of alcohol.

The observation of the effects of anæmia of nerve cells under experimental conditions in which no other complicating factors are introduced, *e. g.,* anæsthesia, and particularly under conditions which permit of repetition, is difficult. The observation of the decapitated animal probably approximates most closely the uncomplicated state of affairs. But repetition under the same or under changed conditions is impossible in the same animal, and it is the spinal cord from which the nerve impulses leading to the motor manifestations arise, and not the brain. In some unpublished obser-

vations on decapitated cats, movements of the fore and hind limbs occurred at varying intervals up to eight minutes after decapitation. They were not continuous, as in absinth convulsions or in general epilepsy as observed clinically, but intermittent. They appeared at varying intervals after decapitation. Their onset was immediate only when the animal has been exercised to the point of exhaustion before decapitation. Nothing was observed in either the head or trunk which compared with the absinth convulsions in continuity, duration, or character. In cerebral anæmia, the phenomena most closely approximating epilepsy were observed during the period of recovery rather than immediately after the occlusion of the arteries to the head. Wilson has urged this delay in the onset of convulsions as an argument against the view of a vascular genesis. We have given elsewhere other objections (Notkin, Coombs and Pike) to the view of a vascular genesis of epileptic convulsions. Closer study will probably show several respects—*e. g.*, the respiratory and visceral changes—in which the convulsions due to curtailment of the blood supply to the brain, or to the injection of absinth, differ from epileptic convulsions as observed clinically.

The method of electrical excitation of the cerebral cortex, apparently first used for this purpose by Ferrier, although according to Hollander he was anticipated by Rolando, has the advantage of inducing convulsions by direct excitation of the cortical cells of origin of the motor fibers without direct excitation of any other part of the nervous system. There is also the advantage of having no extraneous chemical substance present in the nerve cells so that processes of excitation and recovery are the only processes resulting directly from the employment of this method. It was used extensively by François-Franck who recorded blood-pressure and respiration during the resulting convulsion. It has the disadvantage of requiring the administration of an anæsthetic during the time of exposure of the cerebral cortex and the further disadvantage of not being amenable to quantitive measurement. Recently, Zagami has induced convulsions by the application of strychnine to the exposed motor cortex previous to electrical excitation of the corresponding sensory area of the skin. Muncie and Schneider have used this method in conjunction with the administration of absinth.

THE QUANTITATIVE ESTIMATION OF THE DOSAGE OF ABSINTH.

The statement that the method of absinth permits a more exact quantitative measurement than the other methods needs some amplification. The quantitative measurement of any stimulating agent must be given in terms of work done upon the tissue. Stimulation of the retina by green light requires an amount of work equal to 1×10^{-7} ergs, while stimulation of a nerve trunk by condenser discharges requires 1×10^{-4} ergs. We have no means whatever of determining how much work absinth or any other non-ionizing chemical substance does upon the nerve-cells although Benedicenti and Bonino have made some observations upon the relation of the thermodynamic activity of some electrolytes to their biological action. Nor have we any means whatsoever of determining how much work is done upon the nerve cell by curtailment of the blood supply or by electrical excitation in inducing a convulsion. But we can measure the quantity of absinth or camphor monobromide necessary under varying conditions, whereas we have no measure of the quantity of anæmia or of the quantity of electricity. We have no common terms in which to compare the effects or results of the various methods of inducing convulsions. We can merely compare the results of any given method of eliciting convulsions under one set of conditions with the results obtained by that same method under another set of conditions.

Since it is one part of our present purpose to compare the effects of the same drug or other procedure, upon convulsions elicited by various experimental means, some more detailed statement of the results of the employment of each method may be given.

The general response of the organism to absinth or camphor, together with the technique we have adopted for its administration, have been given elsewhere. Wherever it has been possible to do so, we have tried to avoid some of the evils of the purely statistical method by determining the minimal convulsive dose of absinth under control conditions in each experiment before introducing any modification of these conditions. But since it is not possible wholly to dispense with the statistical method it seems desirable to present some data on the minimal convulsive dose of absinth in animals on which no experimental procedure involving the central nervous system had been attempted and in which, post mortem, there were no obvious signs of disease.

One method of determining the minimal convulsive dose of absinth is to inject intravenously into an animal about the same dose which we have previously found to be effective in other animals. It became apparent, however, rather early, that there were certain limits of variation in animals which appeared to be otherwise in healthy condition. A more accurate method was to weigh the animal with a reasonable degree of accuracy—to ounces at least, and perhaps, also, to fractions of an ounce—and then taking advantage of previous experience, to start with some dose lower than that of the minimal convulsive and gradually increase this dose until the clonic twitches appearing after the lower doses, merged into a sustained series which could be accounted as a full-fledged convulsion. After the determination of this minimal convulsive dose, hypotonic and hypertonic solutions and various drugs could be injected intravenously and the minimal convulsive dose determined under the changed conditions.

The results of such determinations may be presented graphically. In Fig. 1, the total dosage of absinth in hundredths of a cubic centimeter is given in the vertical axis at the left and the weight of the animal in pounds and kilograms is shown on the horizontal axis at the bottom. The position of any given circle is fixed with reference to the two coordinates—total dosage required to produce a convulsion as determined experimentally, and body weight as determined by the scales. For example, if a cat weigh 10 pounds, and requires a total dose of 0.35 cc. of the standard solution of absinth to produce a convulsion, a circle is drawn at the point of intersection of the vertical line drawn through 10 on the horizontal axis with the horizontal line drawn through 0.35 on the vertical axis. The procedure for any other dosage and weight is similar.

The results of over 250 such determinations of the minimal convulsive dose appear in Fig. 1. The fan-shaped distribution of the circles on the graph gives the impression of a rather wide scattering of the dosage, particularly for the higher weights. But this scattering is more apparent than real. If lines are drawn through the point of origin of both horizontal and vertical axes, to pass through the intersections of the vertical through 10 on the horizontal axis with points opposite .15, .20, .30, .35, and .40 on the vertical axis, these lines will mark the points on the graph at which the minimal convulsive dose has the value of .015 cc., .020 cc., and so

per pound of animal. It will be observed that by far the greater number of circles on the graph lie between the lines along which the value of the minimal convulsive dose is between .020 cc. per pound and .040 cc. per pound. Owing to the large scale on which the graph was drawn, animals weighing more than 10½ pounds are omitted.

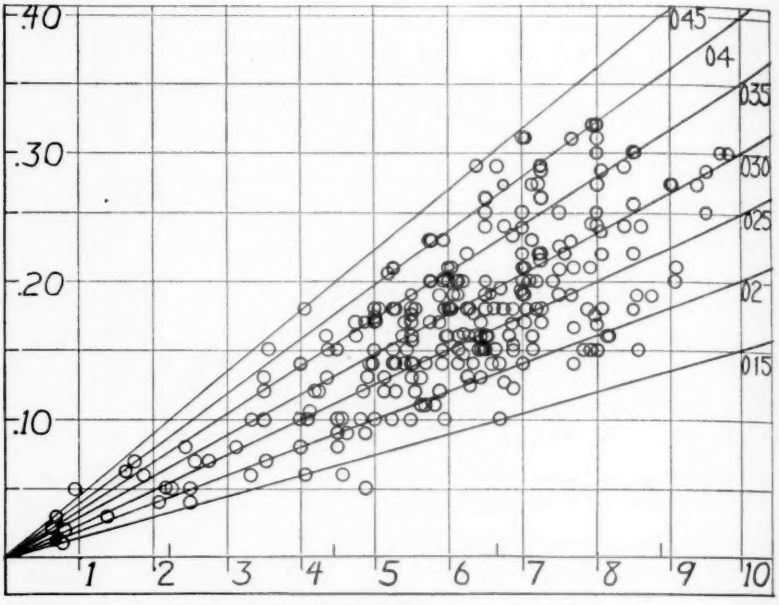

FIG. 1.—The distribution of the total amount of absinth in cc. necessary for the minimal convulsive dose according to the weight of the animal (cats). The total dosage is given in fractions of a cc. on the vertical axis at the left. The weight is given on the horizontal axis. The numbers and the divisions below the axis are in pounds. The divisions above the axis are in kilograms. The diagonal lines marked .015, .02, .025, .030, .035, .040, and .045 respectively represent the dosage in cc. per pound at any point on the line. Each circle in the diagram represents one animal.

The minimal convulsive dose may be reduced to fractions of a cubic centimeter per pound by dividing the total dose for any given animal by the weight of this animal. When plotted according to the minimal convulsive dose per pound and total weight, as in Fig. 2, we find that the apparent scattering of the animals of higher weight in Fig. 1 disappears. There is no apparent constant variation of minimal convulsive dose with weight, although the

number with the lowest (less than one pound) and highest (more than 10 pounds) weight is not as great as for those of medium weight (four to eight pounds).

From the data used in the construction of Fig. 2 we may make the ordinary statistical curve of the distribution of the animals according to the minimal convulsive dose, as has been done in Fig. 3. If we indicate each individual animal by a circle, the number of circles appearing to the right of the decimal corresponding to the fraction of a cubic centimeter for any given minimal convulsive dose per pound, *e. g.*, .030 indicates the number of ani-

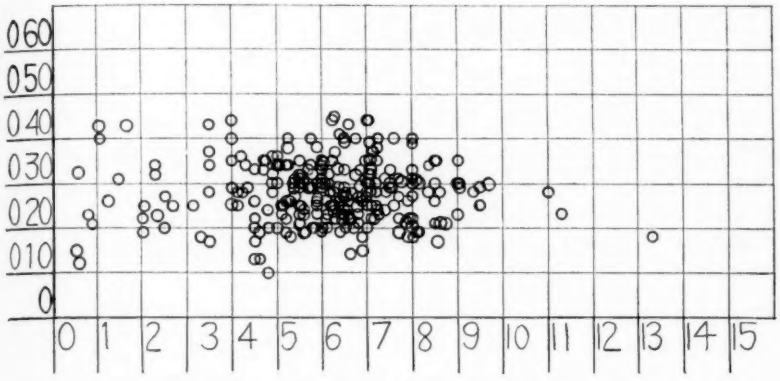

FIG. 2.—The distribution of animals (cats) according to total weight and minimal convulsive dose of absinth per pound. The dosage in cc. per pound is given on the vertical axis to the left. The weight in pounds is given on the horizontal axis. Each circle represents one animal.

mals in which the minimal convulsive dose per pound was of the magnitude indicated by the decimal at the left. In this figure the apparent scattering in Fig. 1 has vanished.

Some aberrant results appear in Figs. 2 and 3. For example, in Fig. 3 the series is continuous for minimal convulsive doses from .016 per pound to .040 per pound. But there are seven more or less isolated cases represented by circles lying below .015 per pound and nine lying above .040 per pound. This break in the series is more apparent in Fig. 3 than in Fig. 2. One of the animals showing an abnormally low minimal convulsive dose—.015 cc. per pound—had received an injection of typhoid vaccine four days before the injection of absinth. But another animal in which the minimal convulsive dose was the same had no discoverable internal condition and

no known previous history to account for the low convulsive threshold. Nor was there any discoverable condition, apart from a large thymus, in the animal showing the lowest convulsive dose of all—.01 cc. per pound—to account for its isolation. Nor was there any discoverable condition in the group of animals represented by the

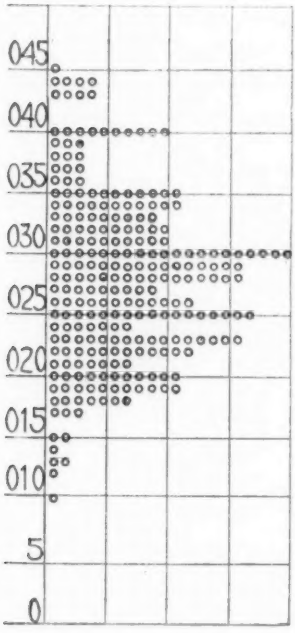

FIG. 3.—The distribution of control animals according to the minimal convulsive dose of absinth in cc. per pound. The minimal convulsive dose in cc. per pound is given on the vertical axis. The number of circles, each representing one animal, to the right indicate the number of animals in which the minimal convulsive dose was of the magnitude indicated on the vertical axis. The total number of animals was 219. The peak lies at .029 cc. and .030 cc. per pound.

circles lying above .040 in Fig. 5 to account for their relatively high threshold to absinth.

Pathological Animals.—Some apparently constant relations between the magnitude of the minimal convulsive dose and the physical type of the animal were noticed. In all animals in which the walls of the internal saphenous vein were thin, with rather free hæmorrhage after each puncture with the hypodermic needle, the minimal convulsive dose was low, ranging from .016 to .025 cc. per

pound. Such animals almost always had a larger thymus than one would expect from the size of the animal itself, and, frequently also, the spleen was large. A large thymus without thin-walled veins was not so commonly associated with a low threshold for absinth. In one animal in which the spleen was about three times its normal size, *i. e.*, 7.5 inches long as compared to 2.5 inches, the minimal dose was low.

There is some indication of a bimodal curve of distribution, with one maximum at .030 cc. per pound and the other at .024 per pound, but the break is hardly wide enough or sufficiently sharply marked to justify making a dichotomy of all the animals into two distinct types. There seem to be intermediate types so far as the minimal convulsive dose is concerned.

Evidences of distinct pathology have sometimes been seen in our animals. Not all of these conditions are associated with any significant change in the minimal convulsive dose. In one animal (No. 967) in which there was a cystic kidney the minimal convulsive dose was .021 cc. per pound, a value which while lying toward the lower limits of the unbroken series still falls within the range as determined from animals in which there was no obvious pathology. In some animals, on the other hand, in which there were distinct lesions in the lungs, no clonic convulsions were obtainable. In experiment No. 951, for example, in which the weight of the animal was 11 pounds and 3 ounces, there were some clonic twitches with bushing of the tail, but no typical clonic convulsion at any dosage. There was some tonic extension of the limbs, although not as marked as usual, at the lethal dose—.033 cc. per pound. At post mortem the stomach was found dilated, with congestion and œdema of the pancreas. The base of the left lung was adherent to the mediastinum which was displaced to the left and there was a consolidated area with a white patch in the region of the adhesion. The lungs were hæmorrhagic about the base of the bronchi.

The errors in the determination of the minimal convulsive dose lie mostly in the errors in reading the dosage and in the estimation of the points at which a real convulsion occurs. In working up from an amount of absinth which produces no noticeable twitches of the skeletal muscles or of the face or ears to the amount at which a sustained convulsion occurs, there will be increasing excitement, cries, struggles, the appearance of moisture on the pads of the feet,

bushing of the tail, and isolated or generalized twitches of the skeletal muscles, before the sustained convulsion finally appears. There is some difficulty in distinguishing the point at which isolated or generalized twitches merge into the sustained convulsion, but the break is fairly sharp. In an animal weighing 6 pounds, there may be only isolated twitches when the total amount of absinth injected is .17 cc., and a good general convulsion when this amount is .19 or .030 cc. per pound. Discarding all beyond the third place of decimals since, although easy to compute, they are of doubtful significance, the difference between a convulsive and non-convulsive dose would be at the most .005 cc. per pound. The error would appear in the third decimal place only. If the animal weighed 5.75 pounds, the dose per pound when the total amount injected was .17 cc. would be only .029 cc. An error of 4 ounces in the weight of the cat is less significant than an error of .01 cc. in reading the scale on the syringe. We consider that Fig. 1, in which total dose and weight are recorded as accurately as they can be determined is the best index of the minimal convulsive dose. The variations in dosage are apparently considerably greater than the errors of measurement. It has been objected that the estimation of dosage according to the weight of the animal cannot be regarded as an accurate quantitative estimation, since it takes no account of the variation in the rate of metabolism with variations in surface of the body. A certain amount of justification must be granted for this objection, but in the present state of development of pharmacology dosage is expressed in terms of weight rather than in terms of surface, in pounds or kilograms rather than in square feet or square meters.

The Experimental Results.

The effects of the injection of hypertonic, isotonic and hypotonic fluids upon convulsions induced by absinth.

The technique of the administration of absinth, as we have employed it (Pike, Elsberg, McCulloch and Chappell) is the exposure of the internal saphenous vein under local anæsthesia, and the direct intravenous injection of absinth followed immediately by a few cubic centimeters of 0.9 per cent solution of sodium chloride. On withdrawing the hypodermic needle from the vein, there is sometimes a small amount of hæmorrhage. Rarely a small branch

of the femoral artery is ruptured, in clearing the fascia away from the vein and a slight hæmorrhage may follow. In order to determine whether or not the introduction of such amounts of fluid or the slight hæmorrhage has any effect upon the susceptibility of the animal to absinth, varying volumes of fluid ranging from 1 cc. per pound to 70 or 80 per pound, have been introduced intravenously and the change in the minimal convulsive dose noted.

In the first experiments upon the introduction of fluids, a 5 per cent solution of sodium chloride was injected intravenously and the minimal convulsive and lethal doses then determined. Both appeared to be raised, or at least to be higher than one would expect from a comparison with the average dose for control animals. The question arose as to whether this increase in the minimal convulsive dose was due to a salt effect or whether it was due to a withdrawal of fluid from the tissue spaces due to the increased osmotic pressure of the blood (Fischer). If the second possibility is the fact, some other hypertonic fluid should have the same effect when introduced intravenously in sufficient volume. The migration of fluid from the tissue spaces to the blood stream might bring about either a decrease in the pressure of the cerebrospinal fluid or a partial dehydration of the nervous tissue itself, or both. A 25 per cent solution of glucose was substituted for the 5 per cent solution of sodium chloride and, after the first few experiments, the technique was changed so that the minimal convulsive dose of absinth under control conditions was determined before the intravenous introduction of any fluid. The determination of the control dose of absinth avoided any uncertainty of interpretation of results based on purely statistical comparison alone. In almost every experiment, the minimal convulsive dose of absinth was raised by the injection of the solution of glucose. We could not determine the lethal dose under control conditions and after the injection of the solution of glucose on the same animal. Hence our opinion as to the magnitude of the lethal dose must be based upon statistical comparison.

Considered purely from the point of view of statistical comparison, the figures for the minimal convulsive doses after hypertonic fluids, as compared with those of control animals, do not afford any adequate basis for saying what the effect of the hypertonic fluid is in any individual animal, nor does the comparison of the graphs of distribution (Fig. 4) of the dosages in the animal before and

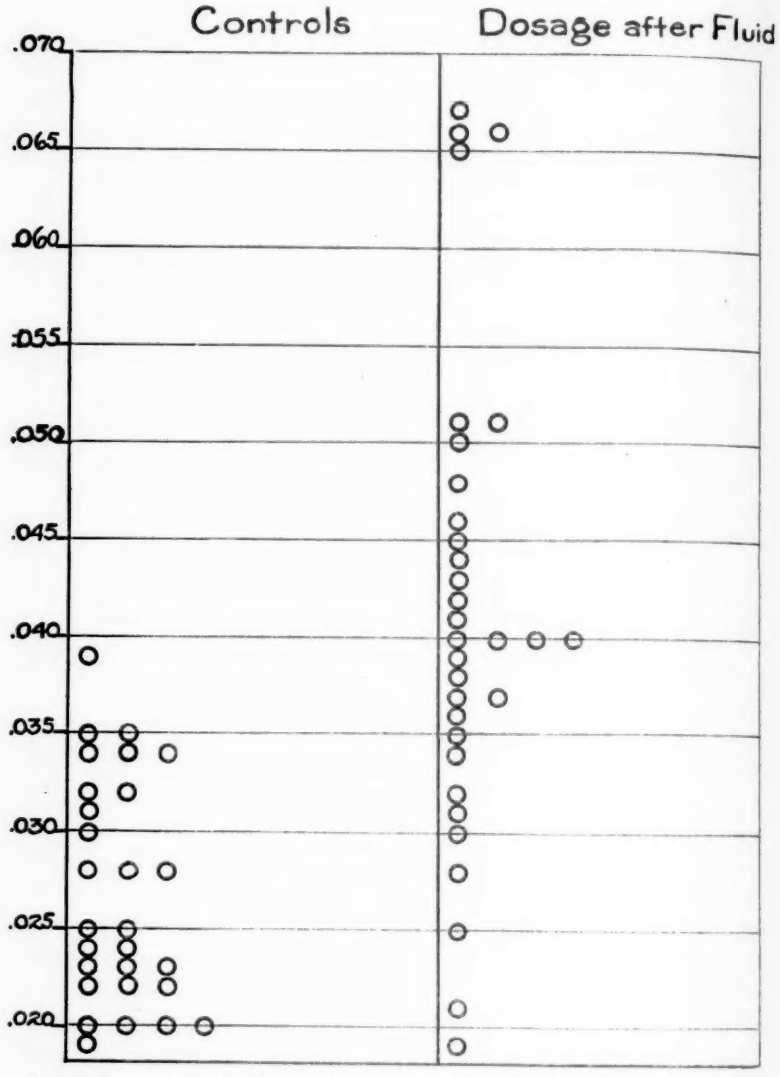

FIG. 4.—Showing the distribution of the minimal convulsive dose of absinth per pound under control conditions (left hand column) and after the injection of varying volumes of hypertonic fluid—solution of glucose or sodium chloride (right hand column).

after the injection of fluid, taken by itself, permit us to say what happens in any individual animal. Such a situation is not entirely new. James Clerk Maxwell, the centenary of whose birth was observed last year by physicists all over the world, remarked, more than half a century ago: " In dealing with masses of matter, while we do not perceive individual molecules, we are compelled to adopt what I have described as the statistical method of calculation, and to abandon the strict dynamical method in which we follow every motion by the calculus."

More recent comment by physicists, notably by Bridgman and by Planck, is to the same effect. While the application of the calculus does not seem called for in the present instance, it is possible to follow, in accordance with the dynamical method, the reaction of each individual animal by the scales and volumetric pipettes.

The tabular representation of the variations of the dosage of absinth with variations in the amount of fluid injected, while possible, is cumbersome and not particularly striking, particularly in those cases in which the level of the convulsive dose was determined several times in the same animal after successive injections of hypertonic fluid. Following Maxwell again, " for the sake of associating the statement of scientific fact with mental images which are easily formed and which preserve the statements in a form which is always ready for use " we present the results graphically in Fig. 5.

In general, the increase in the minimal dose necessary for the production of a clonic convulsion after the injection of the solution of glucose varies with the number of cubic centimeters per pound. It is obvious that there must somewhere be a limit to the amount of glucose which may be injected without causing death from the fluid alone. Those who have injected 25 per cent solutions, or even more concentrated solutions, or sodium chloride, are aware that no very great volume of fluid of such high concentration is required to cause death without any other procedure. In a certain number of experiments, therefore, rather large volumes of the solution of glucose were introduced as soon as the effects of the control dose of absinth had passed off. In some cases, death resulted within three or four minutes after the introduction of the hypertonic glucose. In other experiments, more moderate amounts were introduced at first and the minimal convulsive dose of absinth redetermined. More glucose was then injected and more absinth admin-

istered, and the procedure repeated until the animal succumbed from the injection of the glucose alone. In Fig. 5 the vertical axis at the left indicates the volume of standard solution of absinth in hundredths of a cubic centimeter. On the horizontal axis the num-

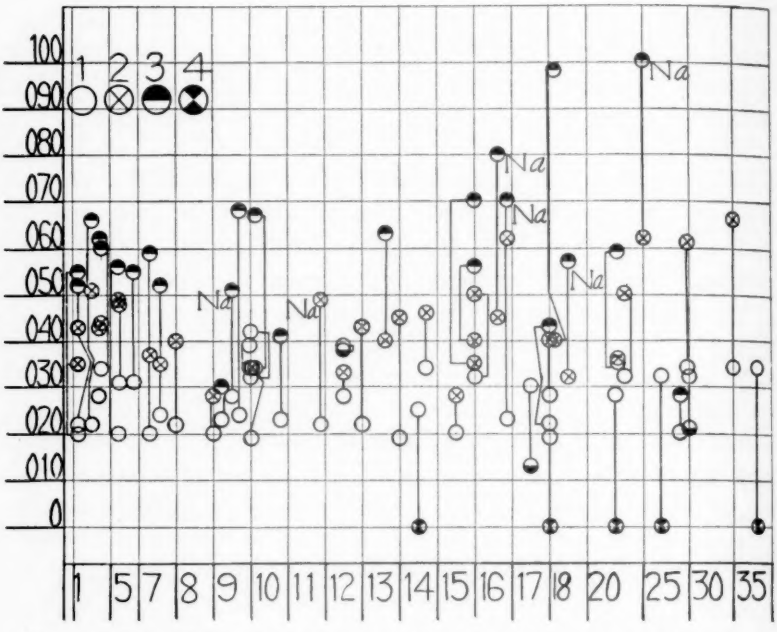

FIG. 5.—The effects of intravenous injection of hypertonic fluids, 25 per cent solution of glucose (unmarked) and of 5 per cent solution of NaCl (marked Na) upon the dosage of absinth.

Explanation of symbols:

1. Open circle, minimal convulsive dose under control conditions.
2. Circle with cross, convulsive dose after injection of fluid.
3. Half filled circle, lethal dose after injection of hypertonic fluid.
4. Quartered circle, death from injection of fluid alone, with no administration of absinth after the fluid was in.

The dosage of absinth in cc. per pound is given on the vertical axis at the left. The volume of fluid injected, in cc. per pound, is given on the horizontal axis.

ber of cubic centimeters of glucose injected per pound is indicated. The scale is spaced unevenly so that in the region of the most frequent dosage the intervals for equal volumes are longer than those at the beginning and end of the scale. This widening of the intermediate spaces was adopted to obviate the inextricable confusion

which would otherwise result from the great congestion of the circles in this middle range. It will be noted that toward the right of the scale, there are some quartered circles on the line indicating the zero dosage but connected by vertical lines with open circles above. These quartered circles represent the death of the animal from the intravenous injection of glucose alone when it had reached the volume per pound indicated by the numerals immediately below. The open circles immediately above indicate the minimal convulsive dose under control conditions. With one exception, it will be seen that the volume of fluid necessary to produce death varies with the minimal convulsive dose under control conditions. The higher the minimal convulsive dose, the greater the volume of fluid per pound which must be injected to cause death. It will be seen also that, with few exceptions, the absolute increase in the amount of absinth necessary to produce a typical clonic convulsion after the injection of the glucose varies with the minimal convulsive dose under control conditions and the volume of fluid per pound injected.

There were only two cases in which the minimal convulsive dose was lowered, as compared with the control dose, after the injection of glucose. These occurred when the volume of fluid injected was equal to 10 cc. per pound. Sometimes the increase in the minimal convulsive dose after the injection of fluid is slight, but such cases are limited to those animals in which the control dose of absinth was below .03 cc. per pound.

The lethal dose of absinth after the intravenous injection of glucose is, in general relatively high until the volume of fluid per pound reaches 16 cc. When amounts of fluid greater than this are injected, the differences between minimal convulsive and lethal doses are not so great, and the lethal dose may even be lowered, as is shown by the half-filled circles below the open circles at volumes of fluid equal to 17 cc. and 30 cc. per pound respectively. It is perhaps worthy of note that only those animals in which the control dose of absinth was equal to .03 cc. or more per pound survived the introduction of more than 25 cc. per pound of the solution of glucose. The limit of safety for most animals would appear to be somewhat lower than this.

Compared on the basis of osmotic pressure, a 25 per cent solution of glucose, expressed in terms of molecular concentration, is 1.38 *M*. Since it does not dissociate, its osmotic pressure would be about

30. atmospheres. A 5 per cent solution of sodium chloride would be equivalent to an .85 *M* solution. Owing to its dissociation in aqueous solution, sodium chloride, in common with other electrolytes, has a higher osmotic pressure than would be indicated by its molecular concentration. The theoretical depression of the freezing point of an .85 *M* solution would be 2.86° centigrade,* corresponding to an osmotic pressure of $\frac{2.86 \times 22.4}{1.84}$ atmospheres, or 34.7. Roughly, the 25 per cent solution of glucose is osmotically equivalent to the 5 per cent solution of sodium chloride, and the effects of the two solutions upon the minimal convulsive and lethal doses of absinth are more or less parallel, so far as present evidence goes.

Information on the remote effects of hypertonic fluids is not very complete. In one animal, 8 pounds in weight, the minimal convulsive dose of absinth under control conditions was .039 cc. per pound. A total volume of 100 cc. of 25 per cent solution of glucose, 12 cc. per pound, was then injected and the animal left for a time. An hour and a half later it was quietly lying on the board, making few movements. It gave the impression of being near a collapse. The respiration was labored. Injection of about the same dose of absinth, .038 cc. per pound, as before was followed by a general clonic convulsion, then tonic extension, respiratory failure and death. Post mortem examination showed considerable œdema in the mesentery, particularly about the pancreas. The liver was spotted in appearance and red in color. The lungs showed many petechial spots. There were some dull, soggy looking patches, particularly about the roots of the bronchi. There was crepitus on palpation, with the escape of some white frothy fluid from the nostrils when the right lung was handled. Pulmonary œdema has been observed in other animals of this series after the injection of large volumes of glucose.

The effects of isotonic solutions, .9 per cent NaCl, and of distilled water or tap water are, in general, less uniform than those of the hypertonic fluids. Large amounts of .9 NaCl can be injected intravenously with safety, unless there is some definite pathological condition present, and intravenous or subcutaneous injection of iso-

*We are indebted to Dr. E. G. Miller for this value, taken from the International Critical Tables.

tonic sodium chloride has long been a routine procedure in the treatment of hæmorrhage or threatened collapse. Hypotonic fluids, however, have been frowned upon under similar conditions. A part

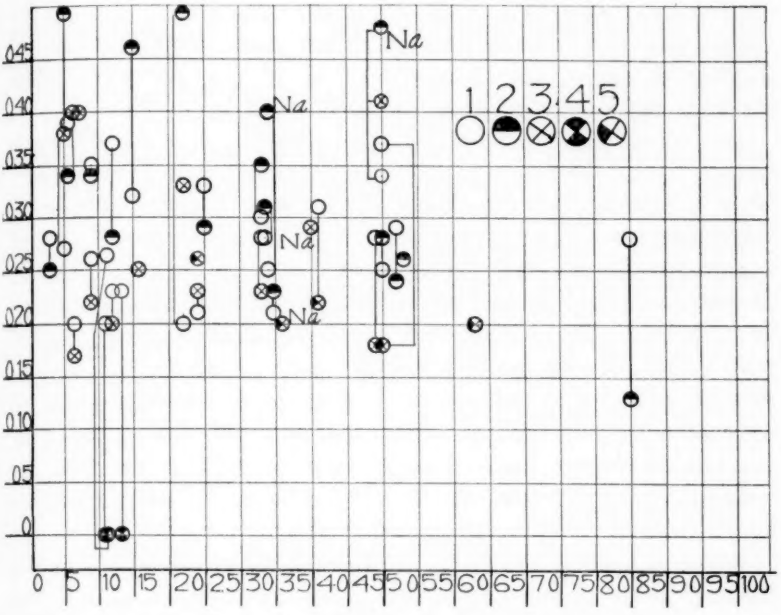

FIG. 6.—The effects of intravenous injection of tap water (unmarked) and of isotonic (.9 per cent) sodium chloride (marked Na) upon the dosage of absinth.

Explanation of symbols:

1. Open circle minimal convulsive dose under control conditions.
2. Half filled circle, lethal dose of absinth after fluid is injected.
3. Circles with cross, minimal convulsive dose after the injection of fluid.
4. Quartered circle, death from injection of fluid alone with no absinth after last fluid was in.
5. Single quadrant circle, minimal convulsive and lethal doses the same.

The dosage of absinth in cc. per pound is given on the vertical axis at the left. The volume of fluid injected in cc. per pound is given on the horizontal axis.

of the literature is given by Cobb, and Ferraro has made a study of the histological changes in the brain.

We shall again follow the methods of dynamics rather than the statistical method in presenting the experimental results (Fig. 6).

The minimal convulsive dose of absinth is, in general, lowered after the injection of tap water, but, in a few animals, it was greater after the introduction of tap water than it was under control conditions. In one animal, in which the control dose of absinth was .027 cc. per pound, the minimal convulsive dose rose to .037 cc. per pound after the injection of 5 cc. of tap water per pound, and, in another animal it rose from .020 cc. to .033 cc. per pound after 22 cc. of tap water per pound had been injected.

In general, however, the minimal convulsive dose of absinth is reduced after the injection of larger volumes of hypotonic fluid. This is particularly true of the lethal dose, which is sometimes significantly less than the minimal convulsive dose under control conditions. In no case did the lethal dose lie above .05 cc. of absinth per pound even when relatively small volumes of fluid—10 cc. to 20 cc. per pound—were injected. Death from injection of fluid alone after the determination of the minimal convulsive dose of absinth, shown by the quartered circles at the line of zero dosage of absinth, occurred at volumes of fluid as small as 12 cc. to 15 cc. per pound in three cases. Occasionally the control dose and the convulsive dose after the injection of fluid were the same, as shown by the circles with one quadrant filled in.

When an interval of an hour or more is allowed to elapse between the time of the injection of a large volume—50 cc. per pound—of isotonic salt solution, and the subsequent dose of absinth, the minimal convulsive dose may be increased, but the lethal dose is not so much affected. In an animal weighing $8\frac{3}{8}$ pounds, the minimal convulsive dose of absinth under control conditions was .034 cc. per pound. Two hours after the injection of 420 cc. of isotonic solution of sodium chloride, 50 cc. per pound, the minimal convulsive dose of absinth was .041 cc. per pound and the lethal dose, 20 minutes later, was .047 cc. per pound.

It is apparently not mere volume of fluid alone which brings about the variations in the minimal convulsive and lethal doses of absinth, but the disturbance of the osmotic relationships from hypertonic or hypotonic fluids. Duryee reports an increase in rate of consumption of oxygen by Planaria and early Amblystoma embryos when placed in Ringer's solution and a decrease when placed in distilled water. The problem becomes one of water relationships (Semper, Rowntree) and there are some indications that the principle of

maxima and minima of physical chemistry (Murray), and possibly Gibbs' phase rule triangle applies here. We will not at this time, however, follow the problem into other fields.

The total amount of absinth, in fractions of a cubic centimeter per pound, which may be injected before causing the death of animals, together with the amount of hypertonic glucose per pound, is given in Table I. It will be observed that in those experiments

TABLE I.

THE MINIMAL CONVULSIVE DOSE UNDER CONTROL CONDITIONS, AND THE TOTAL AMOUNT OF ABSINTH PER POUND AFTER THE INJECTION OF VARYING AMOUNTS OF HYPERTONIC FLUID PER POUND.

Experiment number.	Control dose in cc. per pound.	Total amount of absinth in cc. per pound.	Volume of hypertonic fluid injected in cc. per pound.
682	.04	.2564	4.7
681	.019	.328	3
680	.02	.2696	1.6
673	.03	.32	3.7
672	.035	.352	4
671	.02	.2672	7.3
670	.02	.260	5.9
668	.027	.137	7.7
667	.036	.358	10
666	.03	.069	17.5
665	.035	.2476	22.0
663	.032	.076	30.0
932	.039	.107	12.0
830	.024	.510	9.7
828	.023	.20	10.8
832	.020	.13	9.0
834	.028	.073	12.5
836	.023	.080	9.2
839	.022	.316	8.0
842	.019	.346	18.2
856	.032	.240	27.2
826	.034	.320	30.6

in which the amount of glucose approached the lethal point—17.5 cc. and 30 cc. per pound—the total amounts of absinth were of the order of magnitude of a single lethal dose under control conditions.

In contrast to this we may cite the corresponding results when hypotonic fluids are injected, as given in Table II, and the results for control animals in Table III. The figures on total dosage are

TABLE II.

THE MINIMAL CONVULSIVE DOSE OF ABSINTH UNDER CONTROL CONDITIONS, AND THE TOTAL QUANTITY PER POUND AFTER THE INJECTION OF VARYING AMOUNTS OF HYPERTONIC FLUID PER POUND.

Experiment number.	Control dose in cc. per pound.	Total amount of absinth in cc. per pound.	Volume of hypotonic fluid injected in cc. per pound.
731	.036	.112	11
723	.028	.086	11
687	.040	.231	12
679	.030	.248	5
660	.025	.125	50
659	.029	.119	52
654	.030	.206	33
649	.030	.138	41
640	.037	.142	50
431	....	.530	22
744	.039	.034	5.5
808	.033	.060	25.0
732	.021	.220	35
734	.026	.250	53
738	.023	.080	14.4

TABLE III.

THE MINIMAL CONVULSIVE DOSE AND TOTAL AMOUNT OF ABSINTH IN CC. PER POUND IN A SERIES OF CONTROL ANIMALS.

Experiment number.	Minimal convulsive dose.	Total amount of absinth in cc. per pound.
722	.02	.78
718	.018	.64
714	.015	.215
713	.018	.58
708	.027	.40
707	.024	.26
706	.038	.53
705	.025	.52
699	.026	.38
696	.025	.212
694	.035	.144
676	.035	.30
709	.04	.864
661	.028	.276
645	.035	.287
646	.023	.141
648	.02	.124

subject to so many variations from different conditions that no argument can be based upon them. A considerable number of small doses of absinth may be administered to an animal after the injection of hypotonic fluid in the attempt to find at what volume of fluid per pound the minimal convulsive dose falls to a given level. The sum of these repeated small doses may be greater than that of the few large doses administered to an animal after the injection of hypertonic fluid, although the lethal dose may be low after the hypotonic fluid.

THE EFFECTS OF HÆMORRHAGE AND OF THE INJECTION OF ISOTONIC FLUIDS UPON CONVULSIONS INDUCED BY ABSINTH.

The loss of blood from exposure of the femoral vein, generally less than 1 cc., and the bleeding from the needle puncture during the course of the experiment are so small as probably to be of negligible significance in so far as their effect on the quantity of absinth necessary to elicit a convulsion is concerned. But cranial operations, such as the removal of both motor areas, removal of one entire cerebral hemisphere, or other extensive lacerations of the brain structures can seldom be accomplished without some hæmorrhage. The changes in the concentration of the gases of the blood following successive withdrawals of known amounts of blood have been presented elsewhere (Hastings, Coombs and Pike). Physiologists who have had much experience in the measurement of blood-pressure are aware that no fall of blood-pressure results in control animals from withdrawal of amounts of blood less than one-third of the total volume; and that the intravenous injection of amounts of isotonic saline equal to, or greater than, the volume of the circulating blood does not bring about any significant rise of blood-pressure. After extensive hæmorrhage, the results of intravenous injection of fluid may be different. We have made a few observations on the effects of hæmorrhage, and of the effects of intravenous injections of isotonic saline before or after hæmorrhage, upon the minimal convulsive dose of absinth.

In one animal of $7\frac{1}{2}$ pounds weight, 300 cc. of .9 per cent solution of sodium chloride was injected intravenously and the minimal convulsive dose of absinth—.03 cc. per pound—determined. After withdrawal of 80 cc. of mixed blood and salt solution from the femoral artery the same dose was lethal. In another animal, weigh-

ing 7 pounds, the minimal convulsive dose was .03 cc. of absinth per pound. After the loss of 33 cc. of blood, the minimal dose fell to .024 cc. per pound, and .055 cc. per pound was lethal. In an animal weighing 6¼ pounds, the minimal convulsive dose under control conditions—0.29 cc. per pound—was lethal after loss of 50 cc. of blood. In a fourth animal of 6½ pounds, the minimal convulsive dose was .03 cc. of asbinth per pound under control conditions. The minimal dose was not reduced after loss of 40 cc. of blood. After injection of 130 cc. of .9 per cent solution of sodium chloride, the minimal convulsive dose remained the same. A severe convulsive state lasting several minutes followed .04 cc. of absinth per pound, and .05 cc. was lethal.

Hæmorrhage of significant volume may lower the minimal convulsive and lethal doses of absinth, but the dosage due to hæmorrhage may be repaired in part by the subsequent administration of isotonic solutions of sodium chloride.

THE EFFECTS OF VARIATIONS OF INTRACRANIAL PRESSURE UPON CONVULSIONS INDUCED BY ABSINTH.

The introduction of hypertonic and hypotonic solutions may give rise to various single effects or to a combination of them. There is, first, the effect of variations in the osmotic concentration of the blood itself and the direction of the flow of water between the blood stream and the tissues. An increase in the osmotic pressure of the blood consequent to the injection of hypertonic fluid would be followed by a flow of water from the tissues, where its concentration is greater, since the concentration of substances in solution is less, to the blood-stream, where its concentration is less, due to the greater concentration of substances in solution. The flow of fluid from the subarachnoid and subdural spaces to the blood-stream would result in a reduction of intracranial pressure, as we have stated in an earlier paragraph. The flow of water would be from blood-stream to tissue when hypotonic fluids are injected. As a result, we would have an increase in intracranial pressure as some of this water passed from the blood-stream into the subarachnoid and subdural spaces.

But the process, in all probability, does not end here. Water would leave or enter the cells surrounded by the body fluids, and we would have the effects of dehydration or hydration added to those

of the changes of pressure. Dehydration of nerve-cells and fibers would accompany a reduction of intracranial pressure, and hydration an increase. We have no independent measurement of the effects of either changes of pressure or changes in the water content alone. Some independent method of inducing changes in intracranial pressure seems desirable.

We have previously reported some experiments in which vaseline or paraffin was injected extra-durally through a small hole in the skull (Elsberg and Pike). The minimal convulsive and lethal doses of absinth in these animals were low, as judged by comparing with the statistical results. In some cranial operations, the animals became infected with a gas bacillus so that the skin over the vault of the cranium was tightly stretched. Absinth was injected intravenously in a number of such animals before the skin of the head was incised, and again a few minutes after the incision. The minimal convulsive dose was lower before the incision of the skin, with the escape of foamy pus, than afterward.

In one animal the skull was trephined on the left side under general anæsthesia just back of the cruciate sulcus, and a cork pierced with a short piece of glass tubing fitted tightly in the trephine opening. The ether was then intermitted. The minimal convulsive dose of absinth—.035 cc. per pound—was then determined. A pressure bottle filled with water was connected to the glass tube in the trephine opening, and a pressure of 30 inches of water communicated to the cranial cavity 15 minutes after the injection of the minimal convulsive dose of absinth. Two generalized twitches occurred at once.

A few minutes afterward, under a pressure of 10 inches of water, .022 cc. per pound of absinth was injected. There were immediate generalized twitches, which increased in frequency and violence as the pressure was raised to 13.5, 15, 16.25, 17.5 and 19.75 inches of water. Another dose of absinth—.022 cc. per pound—was then injected with the pressure at 23.5 inches of water. Several generalized twitches followed, with the typical absinth cry. The rubber connecting-tube then slipped off so that the external pressure fell to zero. The animal immediately relaxed and became calm.

At a pressure of 35 inches of water, .029 cc. of absinth per pound was injected. This was followed by a general clonic convulsion which became tonic when the pressure rose to 49 inches. Clonic

twitches persisted for a brief interval after the cork was pulled out of the trephine opening. Some fluid which had entered between the dura and the inner table of the skull escaped slowly and the animal became quiet. With no external pressure, a subsequent dose of .037 cc. per pound of absinth was lethal.

Although the method of varying intracranial pressure by mechanical means avoids any direct hydration or dehydration of the nervous tissue, we cannot say that we have changed one and only one condition. For, as has been known for some years, changes in intracranial pressure are related, in their turn, to general cardiovascular changes (Cushing), an increase of intracranial pressure being paralleled by an increase in systemic blood-pressure. The fact is that it is extremely difficult to change one, and only one, condition in a higher animal organism by any experimental procedure. The living organism in general, and mammalian organisms in particular, afford interesting and complicated illustrations of the theorem of leChatelier (Pike) in their reactions whereby they tend to neutralize any constraint imposed upon them.

THE EFFECTS OF THE INJECTION OF HYPERTONIC AND HYPOTONIC FLUIDS UPON THE REACTION TO CEREBRAL ANÆMIA.

Control animals, as has been shown in previous experiments (Winkin, Coombs) will withstand from 10 to 18 successive temporary occlusions of the head arteries before succumbing to the effects of interruptions to the blood supply of the brain. While the length of the single continuous period of complete occulusion beyond which the animal will not, in general, recover permanently is about 20 minutes, the total period of complete anæmia may be extended to 30 or 40 minutes by making the single occlusion periods two or three minutes each, and allowing a sufficient interval of recovery—15 to 20 minutes—between occlusions.

In the present series of experiments the cerebral arteries were ligated temporarily. A control occlusion was done in each animal and then 10 cc. per pound of 25 per cent solution of glucose was injected intravenously. In no case were there more than five subsequent occlusions and recoveries. The greatest total time, including that of the control occlusion, was 14 minutes. The results are summarized in Table IV.

TABLE IV.

THE REACTION TO CEREBRAL ANÆMIA AFTER THE INJECTION OF HYPERTONIC GLUCOSE SOLUTION.

Experiment.	Number of occlusions, including control.	Weights of animals.	Total occlusion time in minutes.	Amount 25 per cent glucose per pound.	Maximum height control.	Bl. pr. after injection of glucose.
A.....	3	7½ lbs.	7	10 cc.	230 mm. Hg.	230 mm. Hg.
B.....	6	4½ (young animal)	14	10 cc.	185 mm. Hg.	220 mm. Hg.
C.....	4	7½	9	10 cc.	200 mm. Hg.	220 mm. Hg.

In all animals the reaction in the control occlusion was vigorous. This was true also of the first occlusion after the injection of the glucose. But both blood-pressure and cardiac changes soon fell off in magnitude, and the vagus effect, shown in the low pulse rate, became prominent. The changes in the fourth and six occlusions, as compared to the control, in the one animal which was able to stand that many, are shown in Table V.

TABLE V.

HEART RATE AND BLOOD PRESSURE DURING CEREBRAL ANÆMIA AFTER THE INJECTION OF HYPERTONIC GLUCOSE SOLUTION.

	Number of occlusion.	Before occlusion.		20 seconds after occlusion.		60 seconds after occlusion.	
		Blood-pressure.	Heart rate.	Blood-pressure.	Heart rate.	Blood-pressure.	Heart rate.
Control occlusion.	I	100 mm. Hg.	230	80	210	180	240
(After injection of glucose.)	IV	60	200	80	120*	180	240
	VI	40	230	70	130*	100	220

* Vagus effect.

The introduction of 33 cc. per pound of tap water in one animal, subsequent to the control occlusion of the head arteries, reduced the number of occlusions which could be obtained thereafter to one. The rise of blood-pressure was as great in this as in the control occlusion, but no recovery occurred afterward.

In all the animals in which hypertonic or hypotonic fluids were injected, the first occlusion of the head arteries subsequent to the injection was followed by violent reactions of the skeletal muscles.

The general picture of the cardiovascular and respiratory changes attending the introduction of large volumes of isotonic or hypotonic fluids into the stomach has been given in an earlier paper (Coombs).

THE EFFECTS OF THE INJECTION OF HYPERTONIC FLUIDS UPON THE REACTION TO ELECTRICAL EXCITATION OF THE CEREBRAL CORTEX.

We have found that control animals will withstand 40 to 50 successive excitations of the cerebral cortex. The skull is trephined and the region of the cruciate fissure of the cerebral hemispheres exposed under ether anæsthesia. The dura is incised and the anæsthetic intermitted. The animal is kept on the operating table by tapes attached to the limbs and by bands of cloth passed about the neck and just back of the fore limbs. For control experiments no further procedure is necessary except to apply electrodes to the cruciate area of the cerebral cortex and stimulate periodically for 20 to 30 seconds each time with an alternating induced current (tetanizing). The onset of the convulsions is more sudden than after the injection of absinth or temporary ligation of the cerebral arteries, and the convulsive movements in general persist for some seconds after the cessation of stimulation. The effect of hypertonic fluids is to reduce the number of successive electrical excitations of the cortex which an animal can withstand. In two animals in each of which 10 cc. per pound of 25 per cent solution of glucose were injected, the number of successive electrical excitations before death was 20 and 29, respectively. This is significantly less than the usual limits in control animals, although the amount of fluid injected was below the breaking point for any other animals of the series; but it was an amount of fluid which, in other animals, had a significant effect in increasing the minimal convulsive dose of absinth.

The convulsions in these animals were violent, and the clonic twitches persisted 30 to 60 seconds after stimulation of the cortex ceased.

THE EFFECTS OF INJECTION OF HYPERTONIC FLUIDS UPON THE REACTION TO ELECTRICAL EXCITATION.

We have only one experiment upon this point at present, but that one seems sufficiently significant to mention here. Three hundred and fifty cubic centimeters of tap water were injected into the

femoral vein of an animal weighing 10 pounds and 3 ounces, after the first control excitation of the cortex. The experiment (No. 938) lasted continuously from 10.35 a. m. to 4.22 p. m., during which time the cortex was stimulated 80 successive times at intervals of 3 to 8 minutes. The convulsions were not as violent as in control animals or in animals after the injection of hypertonic glucose, and the after effects, *i. e.*, the twitches and other movements, persisted from 10 to 20 seconds, or were wholly absent after the cessation of stimulation. The tail was strongly bushed and there was ocular nystagmus. There was also copious moisture on the pads of the feet.

The experiment was terminated at 4.25 p. m. by the injection of a total dose of .15 cc. (about .015 per pound) of absinth. Tonic extension, cries, and death followed, although the amount of absinth was less than is usually necessary for a convulsive effect in control animals.

Post mortem examination showed moderate ballooning of the stomach, a small thymus, and numerous petechial hæmorrhages in the lungs.

The results were in partial agreement, at least, with those reported by Tower, who found no increase of excitability of the cerebral cortex to electrical excitation under increased intracranial pressure. It is diffiult to see how there can be any significant increase of intracranial pressure when the skull is opened sufficiently to expose the cruciate fissure. The effects in our experiment would seem to be due more to changes in the water content of the tissues than to a change in intracranial pressure. But the change, of whatever nature, did not reduce the number of cortical excitations which the animal could withstand. On the contrary, this number was about 60 per cent greater than that for most control animals.

THE BROMIDES.

The Effects of Bromides Upon Convulsions Induced by Absinth.—There are two cases to be considered—the first, in which the bromide is injected intravenously a short time before the injection of absinth, and second, when bromides are fed for an interval before the injection of absinth.

1. When bromides are injected intravenously and the effect of absinth tried shortly afterward, that is, within a few minutes to an hour, it is possible to get the control dose of absinth before any

injection of bromides. In this manner, confusion incident to interpretation on the basis of purely statistical results is avoided. In all the acute experiments on bromides, one to two grams of sodium

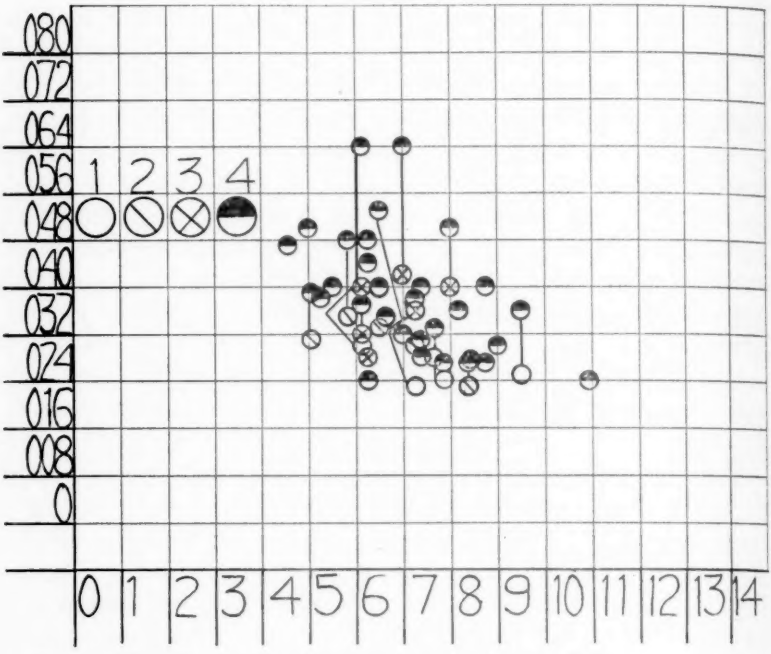

FIG. 7.—The effect of bromides upon the dosage of absinth.

Explanation of symbols:

1. Open circles, minimal convulsive dose of absinth under control conditions.
2. Circle with one cross line, clonic twitches, but no sustained clonic convulsion; after administration of bromide.
3. Circle with cross, minimal convulsive dose after administration of bromide.
4. Half filled circle, lethal dose of absinth after administration of bromide.

The dosage of absinth in cc. per pound is given on the vertical axis. The weight of the animals in pounds is given on the horizontal axis.

bromide were injected from 10 minutes to an hour before the next dose of absinth.

In Fig. 7 the open circles indicate the control dose of absinth per pound before any bromide is injected. The circles with one cross line indicate that clonic twitches occur at the dosage designated.

but without any sustained clonic convulsion after the administration of bromide. The circles with two cross lines indicate the minimal dosage at which a typical clonic convulsion occurs after the administration of bromide. While the half-filled circles indicate the lethal dose of absinth. Reference to Fig. 7 shows that the minimal convulsive dose was raised within an hour after the intravenous injection of bromide.

In one animal in which two grams of sodium bromide were injected immediately before the second dose of absinth, the control dose of absinth was .028. It was only after the injection of three successive doses at intervals of 10 minutes, that a convulsion was obtained at a dosage of .048 per pound, and this dosage was lethal. In a second animal in which two grams of sodium bromide were injected immediately before the second dose of absinth, the control dose was .03 cc. per pound, whereas in 15 minutes, the dose necessary to elicit a clonic convulsion had risen to .04 cc. per pound. No further convulsions occurred until the lethal dose .064 per pound, resulting in tonic convulsions only before death was reached 30 minutes later. The narrowest range between a control dose before the administration of bromides and the lethal dose following the administration of bromides was from .025 as control and .036, characterized by tonic convulsions only before death. The greatest range found was for the second animal—.03 control and .064 lethal.

2. From one-half to one gram of sodium bromide was administered in the food for varying periods ranging from two weeks to three months before absinth was administered. These results are also given in Fig. 7 and in Table VI. No control doses could be given in these animals, and the interpretation must be based upon statistical comparison only. There are in Fig. 7 a number of half-filled circles standing by themselves. These indicate that in the animals to which they correspond, not even clonic twitches were elicitable before death. The first dose which was effective was the lethal dose, and the range is from .024 per pound to .053 per pound for such animals. In other cases, clonic twitches, as indicated by the circle with one cross line were obtainable, but the next dose of absinth might prove fatal. In a certain number of animals, typical clonic convulsions occurred, but the dosage necessary for their elicitation was nowhere greater than .042 per pound and the highest lethal

dose was again .064 per pound. While it seems probable that the administration of bromide for a certain period raises slightly the convulsant dose of absinth, this rise is never very great and the margin between minimal convulsive and lethal doses is certainly not greater than in control animals. Bromides in general do not seem

TABLE VI.

THE MINIMAL CONVULSIVE DOSE AND THE TOTAL AMOUNT OF ABSINTH PER POUND AFTER THE LONG CONTINUED ADMINISTRATION OF BROMIDES.

Experiment number.	Minimal convulsive dose in cc. per pound after bromide.	Total amount of absinth in cc. per pound.
704	.030	.111
703	.035	.207
541	.040	.200
542	.040	.148
544	.030	.150
545	.025	.075
549	.042	.342
551	.035	.220
552	.035	.150
554	.036	.126
599	.030	.064
600	.020	.070
688	.032	.083
688	.025	.163
768	.024	.100
840	.047	.170
852	.028	.152
876	.027	.077
877	.036	.089
886	.027	.20
887	.024	.050
890	.028	.062
897	.027	.070

to be very effective in protecting the animal against the effects of absinth.

The Combined Effects of the Administration of Bromide and the Intravenous Injection of Hypertonic Glucose upon Convulsions Induced by Absinth.—The rather unsatisfactory results of the administration of bromides in protecting against the effects of absinth as compared with the somewhat more satisfactory results of the intravenous injection of hypertonic glucose, suggested the

combination of the two methods. In one cat, weight eight pounds, which had received one gram of sodium bromide daily for about six weeks, the minimal convulsive dose of absinth was .022 per pound. There was a severe generalized clonic convulsion, lasting about two minutes. Seventeen cubic centimeters of hypertonic glucose were then injected into the vein, and the same dose of absinth repeated four minutes after the introduction of the glucose. There was some excitement, but no clonic convulsion. Ten minutes later, a dose of .025 cc. of absinth per pound was lethal. In another cat, weighing 6.125 pounds, which had received one-half gram of sodium bromide daily for a period of 17 days, the minimal convulsive dose of absinth was .032 cc. per pound. Twenty cubic centimeters, that is, about 3 cc. per pound of hypertonic glucose, were injected and the same dose of absinth repeated, without any convulsive effect except cries. The next dose of absinth—.037 cc. per pound—was lethal, with tonic response only.

The Effects of the Administration of Bromides upon the Reaction to Cerebral Anæmia.—The effects of repeated temporary occlusions of the head arteries were studied in animals which had received 1 gram of sodium bromide daily for 10 to 14 days previously. The anæmic response, that is, the rise in blood-pressure, was not as great as in control animals and fewer successive occlusions of two to three minutes each could be done than in controls. The total time, that is, the sum of the successive periods of occlusion, during which the head arteries could be ligated was from 15 to 20 minutes, as against 30 to 55 minutes for control animals. Frequently there was a marked and persistent "vagus effect" characterized by a slow heart rate beginning at about the crest of the initial rise of blood-pressure, persisting through the fall and well up toward the crest of the second rise which occurs in typical form in control animals. The actual increase in the blood-pressure during the period of occlusion was less than was usual in control animals and the period of low blood-pressure associated with cardiac slowing occurring between the initial and the final rises was longer than in controls.

The Effects of the Administration of Bromides upon the Reaction to the Electrical Excitation of the Cortex.—Some of the results of this procedure have been published in a separate paper (Coombs, 1932). The animals had received one-half to one gram of sodium

bromide daily for varying periods of two to six weeks before excitation of the cortex was done. When the amount of bromide administered was as great as one gram daily, 80 or more successive excitations of the cortex could be done before the animal succumbed. No sustained clonic convulsions could be elicited in these animals and sometimes there were not even clonic twitches following excitation of the cortex. When smaller doses of bromide, *e. g.*, one-half gram daily, had been administered, clonic twitches and even mild clonic convulsions were obtainable.

THE EFFECTS OF TRIONAL.

The Effects of Trional upon Convulsions Induced by Injection of Absinth.—All the experiments with trional were acute experiments in which, following the establishment of the minimal convulsive dose of absinth, varying amounts of trional were injected intravenously after which the injection of absinth was resumed. The trional was dissolved in 95 per cent ethyl alcohol in a concentration of .086 grams of trional to 1 cc. of alcohol. The results are shown in Fig. 8. The significance of the symbols employed is the same as in previous figures, the open circles indicating a minimal convulsive dose of absinth in hundredths of a cubic centimeter per pound under control conditions; the circles with crosses, minimal convulsive dose after the injection of trional; and the half-filled circles, the lethal dose. The dose of absinth per pound is given in the vertical column at the left of the figure and the numerals along the horizontal line at the bottom of the figure indicate the total dosage of the solution of trional in hundredths of a cubic centimeter.

The results are, in general, disappointing from the point of view of the protection to the animal from the effects of absinth. In the greater number of experiments, the difference between the control dose, and the minimal convulsive, or even lethal dose, after the injection of trional is not very striking. The two exceptions occurred at total dosages of .82 cc. of the solution of trional when the minimal convulsive dose was raised from .032 per pound under control conditions to .056 per pound, and at 1.12 cc. when the convulsive dose was raised from .032 per pound under control conditions to .068 per pound, respectively. At this higher dosage of

trional, the lethal dose of absinth rose to .11 per pound. More experiments are needed on the effects of these higher dosages of trional upon the incidence of absinth convulsions and also more information upon the time factor, but the data which we now have

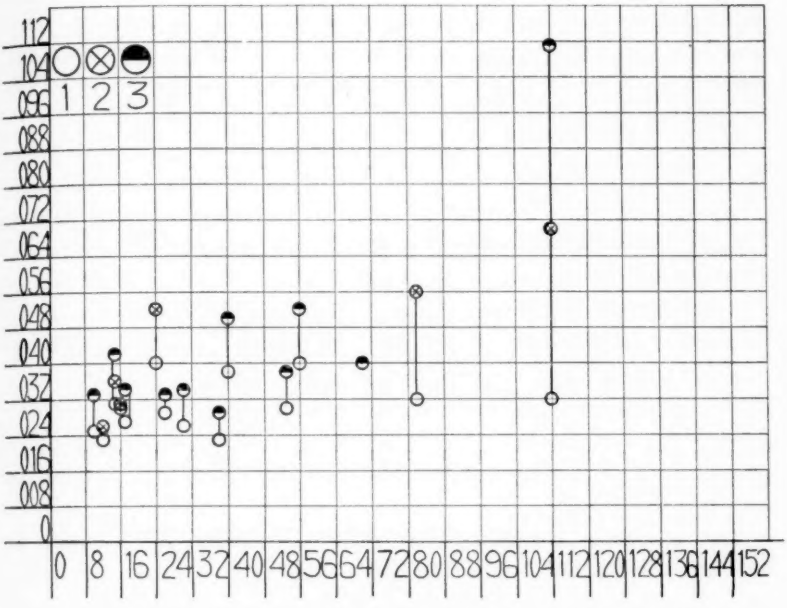

FIG. 8.—Showing the effects of trional upon the minimal and lethal doses of absinth. The dosage of absinth in thousandths of a cubic centimeter per pound is given in the vertical column at the left. The total dosage of the alcoholic solution of trional (.086 grams of trional to 1 cc. of alcohol) in hundredths of a cubic centimeter is given in the horizontal line at the bottom of the chart.

Explanation of symbols:

1. Open circles, minimal convulsive dose of absinth under control conditions.
2. Circle with cross, minimal convulsive dose after administration of trional.
3. Half filled circle, lethal dose of absinth after administration of trional.

are presented for purposes of comparison, with the action of other agents.

The Effects of Trional upon the Reaction to Cerebral Anæmia.—All the experiments upon this phase of the problem have been acute experiments in which trional in alcoholic solution was injected after a control occlusion of the head arteries, and the subsequent occlu-

sions done directly afterward. The cardio-vascular responses to occlusion of the head arteries subsequent to the injection of trional are no longer of the same duration or number as in controls. The greatest number of occlusions which we have obtained subsequent to injection of trional is nine with a duration of one to two and a half minutes each, and a total duration of about 20 minutes. This was in a vigorous young cat. Adult or old animals rarely survive more than four or five short occlusions in which the magnitude of the anæmic rise of blood-pressure was less than in controls.

The Effects of Trional upon the Reaction to the Electrical Excitation of the Cerebral Cortex.—All of these experiments were also acute experiments, in which the trional was injected intravenously subsequent to the first control excitation of the cortical motor area. The number of successive excitations which could be done before the animal succumbed was 70 or more as compared to the 35 to 55 possible in control animals and the total duration of the experiment was five to six hours. In one animal, after 72 successive excitations of the cortex, absinth was injected intravenously in order to terminate the experiment. The lethal dose was .07, and in another animal, after 75 successive excitations of the cortex, the lethal dose was .05 per pound.

The surprising resistance to absinth in these two animals is worthy of note. In control animals, after 35 to 40 excitations of the cerebral cortex, the lethal dose of absinth is low, ranging about .02 cc. per pound. In animals which have received bromides, the lethal dose of absinth is again low .02 cc. or less when injected after repeated electrical excitations of the cortex.

General Comment.

The experimental results show that the same drug or the same experimental procedure may act very differently on convulsions elicited by different experimental methods. In general, the procedure which protects the animal from, or increases its tolerance to, the effects of convulsions induced by one method is not of much value in protecting an animal from the effects of convulsions induced by some other method. This may be brought out more clearly by a tabular summary of the results (Table VII).

In this table, the plus sign indicates that the minimal convulsive or lethal dose, or that the total quantity of absinth is increased, or

that the number of successive occlusions of the cerebral arteries, or total occlusion time, or the number of electrical excitations of the cerebral cortex, as compared to the number or times in control animals, is increased. The minus sign indicates a decrease as compared to the values for control animals, while o indicates that the particular methods after which it stands were not tried under the given conditions, and that we venture no prediction as to what the results would be.

One sees, further, that only one procedure, of those that are given in this paper, is of value in protecting the animal from the effects of absinth, and some may even question the value of that. The injection of hypertonic fluids in certain volumes raises the minimal convulsive dose of absinth, and may also raise the lethal dose.

TABLE VII.

THE EFFECTS OF THE SAME PROCEDURE UPON THE REACTION OF THE ANIMAL DURING CONVULSIONS INDUCED BY DIFFERENT EXPERIMENTAL MEANS.

Method of inducing convulsions.	Specific procedure. Injection of hypertonic solutions.	Injection of hypotonic solutions.	Hæmorrhage.	Increase of intracranial pressure.	Bromides.	Trional.
Absinth	+	−	−	−	−	−
Anæmia	−	−	o	o	−	−
Electrical excitation ..	−	+	o	o	+	+

But the injection of such hypertonic fluids may, in itself, be a source of danger and not only fail to protect the animal from absinth, but even lower its resistance if the volume of such hypertonic fluid rises above a certain limit.

None of the procedures tried are at all effective in protecting the animal from the effects of cerebral anæmia. In other experiments we have found that the intravenous injection of adrenalin, and particularly of ephedrin (Coombs), either with or without isotonic solution of sodium chloride, is of value in protecting the animal from the effects of cerebral anæmia. Adrenalin (Notkin and Pike), however, is not only of no value in protecting the animal against absinth, but is of distinct disadvantage.

The results on electrical excitation of the cerebral motor cortex are more clear. Hypertonic fluids do not protect the animal from the effects of electrical excitation. On the contrary, the number of

successive electrical excitations of the cortex which may be done before the animal succumbs is reduced to one-half or two-thirds of the number withstood by control animals. But hypotonic fluids, so far as our evidence goes, may protect the animal from the effects of electrical stimulation. It may be objected that a small number of experiments is inconclusive. But if one will take the trouble to compute, by Stirling's formula or by any other approved mathematical procedure, the probability that we would get this particular result on the basis of a purely random choice, such a probability would be astonishingly small. The small number of experiments all tending on one direction, acquire significance on a purely statistical background.

The observations on the effects of bromides and trional leave little doubt that these agents are effective in protecting the animal from the effects of electrical excitation of the cerebral cortex.

We are not adducing any of these results as an argument either for or against the validity of any particular hypothesis of the cause of epilepsy. We wish here to present certain facts concerning the effect of certain procedures upon the severity, the number and the threshold of elicitation of convulsions induced by different experimental methods, without much theoretical discussion.

It would seem probable that, when we have a sufficiently exhaustive analysis of the effects of various agents upon convulsions produced by different experimental procedures, and a sufficiently exhaustive study of the effects of various therapeutic measures upon the clinical course of epilepsy, a careful comparison of the two series of results might give us some clearer idea of the nature of the actual cause of epilepsy in the human subject, whether toxic, circulatory or physical, *e. g.*, anatomical, in nature.

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HEREDITARY FACTORS IN EPILEPSY.

A Comparative Study of 1000 Institutionalized Epileptics and 1115 Non-Epileptic Controls.*

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I. Introduction.

Authors have differed widely in their estimates of the extent to which epilepsy is to be found in the antecedents of epileptics; and it has been popularly supposed that the children of epileptics were more likely to develop epilepsy than were those of non-epileptic parents.[1]

This paper presents the results of a tabulation of 1000 complete case histories of patients at the Monson State Hospital for epileptics in Massachusetts during the year beginning October, 1931. To Myerson (28), Davenport (6, 7, 8), and others (Heron, Pearson) may be left the discussion on the relative merits of history-taking by physicians and social workers. These histories were obtained at the time of arrival by the admitting physician from the parent or guardian who usually accompanied the patient to the hospital. The information was usually supplemented by our psychiatric social workers who in most instances visited the homes and obtained pertinent additional data from relatives and interested social agencies.

These 1000 records were studied for the incidence of seizures, migraine, feeblemindedness, alcoholism, psychosis, and other neuropsychiatric disorders in the parents, siblings, children and other relatives of the patients.

The histories cover admissions during the past 30 years; although most of the records that were from 10 to 15 years old or more were ruled out because the data was usually incomplete for our purpose

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[1] It is well to recall primarily the introductory remarks of Hodskins *et al* (14) on the recognition of "epilepsy as a symptom-complex associated with a variety of superficially unassociated conditions" and not as a disease entity *per se*.

and could not be checked up. Records in which all of the immediate family was accounted for, and which included a reasonably complete report on the other relatives, were accepted for this study; and no other basis for selection was used. The records were taken in alphabetical order from the active files of the hospital, and nearly equally distributed between the sexes, there being 486 males and 514 females.

Similar records from a control group of 1115 non-epileptic individuals, who had themselves never had a seizure, were tabulated for the comparative incidence of seizures and migraine in their respective family histories; and 722 of these were studied for the incidence of the other neuropsychiatric disorders, viz., feeblemindedness, alcoholism, psychosis, and miscellaneous neuropsychiatric diseases in the same relatives.[2] Three hundred and ninety-three of these 1115 control histories were made available, through the courtesy of Dr. Wm. G. Lennox of the Harvard Medical School and the Neurological Department of the Boston City Hospital, from questionnaires made directly to nurses and medical students. The remaining 722 were obtained through the generous cooperation of a number of the superintendents of state hospitals in Massachusetts, and of scores of other interested professional and lay people, including physicians, teachers, and social workers. Comprehensive printed questionnaires were sent to these people with the request that they be distributed at their discretion among the members of their staffs, nurses, attendants and friends. The forms were marked "Confidential, Answer in Privacy"; and stamped self-addressed envelopes were supplied with each form, so that the record could be returned directly to the writer. No signature or other identification was asked for, except sex, age, and occupation.

Both sexes, most classes, professions and trades, and practically all ages from 1 to 70 are represented in this study. Of the 1000 epileptics 486 were males, 118 were or had been married; and 87 had had children. Nine hundred and forty-five of these patients had brothers or sisters while 55 were themselves only children, *i. e.*,

[2] Results obtained in the 1115 group of percentages calculated were found to tally within one-half of 1% with those found for the smaller group of 722 records; and results in the 1000 epileptic group tallied similarly within one-half of one per cent with the 612 epileptic group as originally presented; hence we feel that any comparison between the two groups, or between any numbers over 600 or 700, is perfectly rational, and approximately correct.

had no siblings. The total number of siblings was 4305, including 34 half-siblings; and the total number of children was 267; while the total number of parents, siblings and children was 6572.

In the control group two sets of figures are noted. The larger number of 1115 controls were tabulated for seizures and migraine in their immediate families only; and consisted of the following statistical data: males 427, females 672, sex unstated 16, married 324, controls with offspring 175, controls with siblings 997; total siblings

TABLE I.

COMPARATIVE AGES OF 1000 PATIENTS AND 790 CONTROLS.[2]

Ages.	Patients.		Controls.	
	No.	%	No.	%
1 to 5 inclusive	66	6.6	8	1.0
6 to 10 inclusive	169	16.9	14	1.8
11 to 15 inclusive	197	19.7	12	1.5
16 to 20 inclusive	172	17.2	129	16.3
21 to 25 inclusive	109	10.9	218	27.6
26 to 30 inclusive	86	8.6	121	15.3
31 to 35 inclusive	58	5.8	72	9.1
36 to 40 inclusive	46	4.6	61	7.8
41 to 45 inclusive	31	3.1	43	5.4
46 to 50 inclusive	18	1.8	36	4.6
51 to 55 inclusive	19	1.9	31	3.9
56 to 60 inclusive	18	1.8	28	3.5
61 to 65 inclusive	8	0.8	14	1.8
66 to 70 inclusive	2	0.2	2	0.3
70 to 75 inclusive	1	0.1	1	0.1
Totals	1000	100.0	790	100.0

4381 (including 9 half-siblings), total children 456, total parents reported on 2222 (1115 fathers and 1107 mothers), total parents, siblings and children 5959.

The data for the smaller group of 722 controls[2] is as follows: males 205, females 501, sex unstated 16, married 267 and 139 of them had children, controls with siblings 644; total children 315, total siblings 2925 (including 9 half-siblings), total parents, siblings and children 3684.

Table I presents the comparative ages of the patients and controls used in this survey.

Explanation of Table I.—Table I presents from left to right—1st, the ages in 5 year periods; 2nd, the number of patients belonging in the respective age groups, and their percentage of the total number of patients; 3rd, the comparative number of controls in the same age groups, and their percentage of the total 790.[2]

Comment on Table I.—A glance at Table I reveals that the largest number of patients, viz., 583, were between 6 and 20 years of age at time of first admission to the hospital, while the largest number of controls (468) were between 16 and 30 years of age.

It is obvious that a comparison between the individual life histories of the patients and controls would be unfair because of the difference in the age groups; but this difference should in no way affect the validity of their family histories. If anything, in fact, the family histories of the controls should be the more valuable because of the longer period of observation by a generally capable group.

Other interesting data noted during the survey of the past year include the matter of alcoholic intoxication at the time of conception of patients, Section VIII; a group of 27 cases with observations on three generations with seizures, Table VIII, Section XII; and the following data which are in preparation for subsequent presentation: 1—a study of the assigned etiological factors other than heredity in 898 epileptics, including birth trauma; 2—the number of first-born patients in a group of 770 epileptics; 3—the matter of consanguinity in parents; and 4—a study of the ages of onset of seizures.

II. Family Histories.

Concerning family histories, it must be remembered that accurate histories are practically impossible to obtain because they come essentially from the memory of the person or persons telling the story. It is common knowledge to every historian that these stories are often colored by prejudices towards one side of the family tree; that they present the elements of human weaknesses evidenced by attempts to cover up shortcomings and defects so that in a generation or two much valuable information is permanently lost; and also that these accounts are apt to change on different occasions even when given by the same person. Burr (3) appropriately points out that a study in heredity, to be of value, should include all data both positive and negative for at least three full generations, some-

thing that is quite beyond the power of memory for most people, even if all of the data were actually known. Thom (37) and Minkowska (25, 26) have succeeded in doing this but only for a limited number of cases (see below Section IV) and in our own study, too, there were a small number of cases of three generations with seizures (Table VIII—Section XII). The criterion in our selection was that all members of the immediate family, *i. e.*, parents, siblings and children, must be accounted for, and that most of their personal history be made known to the historian. Incomplete family histories were omitted from this study regardless of the apparent wealth of material in what was given.

The contention of Stüber (35), Cobb (4) and others, that because many of the data presented in the literature are for institutionalized cases, such data do not necessarily apply to the class of patients seen in private practice, since the heredity in the two sets of cases may be different, does not seem to us (13) to be well-founded.

In the first place, every institutionalized case was once a private or clinical patient before being referred to the hospital; and in the second place, the social service department of this, as of most large institutions, is usually suitably prepared (because of time and funds for traveling to homes, schools, etc., in all parts of the state) for the task of sifting out accurate first-hand information on histories from places and people outside of the one or two informants that usually furnish the data to the admitting physician of the clinic or private office. Moreover, state hospitals are fed from the general population of the community, from the clinic, and from the private physician; and since the history seldom comes directly or exclusively from the patient alone, which would change its value, it is difficult to understand the antipathy of many writers to this allegedly special brand of institutionally-hatched patients with their supposedly "different" heredity.

"Much of the present-day misconception concerning epilepsy," writes Lennox (19), "arises from the fact that although only approximately 1 in 20 of the persons subject to recurring seizures are in institutions, information concerning these piled-together, driftwood human beings has been easily assembled and when published has been accepted as representing all persons afflicted with seizures."

A few differences one does note: In the first place, institutionalized patients represent a small percentage of the epileptics in the community at large. Secondly, the onset of their seizures seems to occur at an earlier period in their lives than in the non-institutionalized groups. Thus, the average age of onset for our 1000 cases was nine years, with most of them having their first seizure during the first four or five years of their lives, and the next largest group having their onset at puberty.*[3] These figures are identical with the findings of Partridge in 7200 epileptics at Craig Colony (31). Among clinical patients, on the other hand, the greatest number have their first seizure in adolescence. "Approximately a third of the patients had their first attack after reaching the age of 20," writes Lennox (19). One other matter, and that is the larger proportion of feebleminded and deteriorated epileptics one apparently finds in institutions. Since feeblemindedness is supposed to run in families, and to be associated with epilepsy, it should be reasonable to expect a higher hereditary incidence of feeblemindedness in the family histories of institutionalized groups. What are the facts?

First, "In a large group of non-institutionalized patients the proportion of the members of the immediate family (parents, brothers, sisters, and children) who have had seizures was less than 3%," states Lennox (19). Our own figures for the same relation group was 3.7% (Table II). Not a startling difference.

Second: The incidence of seizures in the parents of 1444 non-institutionalized patients, according to Burr (3) was 2.4%. Our own figures for the same incidence of seizures in the parents of 1000 institutionalized epileptics was 2.9% or only one half of one per cent higher.

Third: While the incidence of feeblemindedness in the immediate families (parents, siblings or children) of our patients was nearly twice as great as for seizures (Table II) it was still only 6.6%.

It is natural, too, that estimates by physicians are apt to be colored by their own personal experiences and observations. Thus Lennox, seeing largely grown children and adults who are more or less in active life, and whose seizures began at a later age, considers

*[3] Unpublished data, in preparation.

that epilepsy need not be entirely incompatable with utility. "As a matter of fact," he writes (19), " the majority of epileptics when given a proper chance, are able to live fairly normal lives."

Crothers, who sees mostly children, believes that many of the epilepsies probably begin in infancy, and are never seen by the neurologist or psychiatrist at all (5) (see quotation below, Section III).

Thus, statistical studies made outside of an institution, or even inside of most institutions, are likely to include only adults or grown children, and to omit the infants.

Here at Monson patients of all ages and both sexes are admitted and the data presented, therefore, are fairly representative.

Moreover, the nature and causes of the epilepsy, that is whether traumatic, organic or unknown, are too often obscure, even in the hands of expert investigators, so that it has been found expedient not to attempt a classification of cases for this study into organic and the disputed so-called idiopathic groups.

The one thing of which we can be certain is that all of the cases in this group do have the clinical symptom-complex known as epilepsy.

III. The Incidence of Epilepsy.

There is no unanimity of opinion on the incidence of epilepsy in the general population. Davenport (6) reports the incidence of epilepsy at 1 in 194 or 0.5% among the drafted men of the U. S. army during the world war. Muskens (27) finds it varying from as much as 1 in 200 (0.5%) in France in 1850 to as little as 1 in 1500 (0.07%) of the general population. In Switzerland he found an incidence of 1 in 200 (0.5%), while in Holland it varied from 1 in 300 (0.3%) to 1 in 1800 (0.06%) in 1918. Cobb (4) reports the general incidence of epilepsy at 3 per 1000 or 1 in 333 (0.33%) of the general population; and Hodskins *et al* (14), in a survey of cases in Hampden County in 1922, found 827 epileptics in a population of 327,856, or an incidence of about 1 in 400 (0.25%). Crothers (5) believes that inasmuch as many epileptics die in infancy from birth injuries or early infections the incidence of epilepsy may be higher than most estimates give. " I think it is fair so say," writes Dr. Crothers, " that many children, who have convulsive attacks, die before they reach an age when institutional treat-

ment is recommended. On the whole, this mortality is very difficult to get in any figures since the immediate cause of death is often only indirectly related to the convulsions, so that the convulsive attacks do not appear on the death certificate. This same difficulty arises, I think, with grossly feebleminded children and especially with mongols." Malzberg (24) states: "The rates of first admissions to epileptic institutions in the U. S. have increased since 1922"; but he believes the increases are probably accounted for by increased institutional facilities.

IV. Heredity in Epilepsy.

Most of the older writers, including Oppenheim (29), Gowers (12), Echevaria (9), Binswanger (1) and others, consider heredity to be one of the most important factors in the causation of epilepsy. "A number of conditions are capable of producing it, they agree, but apparently they make their influence felt chiefly when the morbid predisposition is already present" (28). Most of these writers hold the opinion that a hereditary tendency to epilepsy may be found in about one-third to one-half of the cases (Binswanger) and some go as high as three-fourths (Finht). But, as Myerson aptly points out (28)—"These authors are most of them old authors who firmly believed that insanity was a unit, did not know of the origin of general paresis, and syphilis, believed that tuberculosis was inherited, made much of the scrofulous constitutions, spoke about alcoholism as a neuropathic trait, and in no cases had any control figures as to the ancestry and relatives of the normal non-epileptic population."

Brain (2) in 200 patients with epilepsy, found a family history of convulsions in 28% as compared with 10% in a control series of non-epileptics.

Echeverria (9) in a study of 351 children of 136 married epileptics (62 males and 74 females) found that 195 died in convulsions and 78 became epileptics. Therefore, 273 or 51% had seizures of some sort. Thom (36) and (37) in a similar study of 553 children of 136 married epileptics found only 10 with seizures, or 2%.

Davenport (6) believes that epilepsy is a hereditary disease. His conclusions are that when both parents are epileptic or feeble-

minded, all their offspring are so likewise,[4] that normal persons who have epileptic offspring usually show gross nervous defect in their close relatives; that no epileptic transmits like a normal, and that epilepsy is a hereditary Mendelian character due to a defect in the germ plasm. He (Davenport) (7, 8) traces, among many other interesting cases, some of the members of the family of a shiftless laudanum addict who married a disorderly woman, considered epileptic, and mentally defective. This couple had seven children, only four of which are accounted for, and three of these had seizures. These figures are highly suggestive in themselves; and in our own group, too, there are a few cases with two or more of the children and siblings who have had seizures, or have been feebleminded; but these are exceptional as the figures indicate (Table II). As often as not, there have been in such families one or two brilliant siblings who have achieved industrial, scholastic or professional distinction. Moreover, psychopathic narcotic addicts, and mental defectives do not make up the bulk of the parents of our 1000 cases who represent a fair cross-section of all strata of society in Massachusetts.

Thom (37) in his study of 157 cases at Monson in 1915 found 21 cases in which three generations were represented for study. His data are as follows:

1. Twenty-one cases with epilepsy in the patient and epilepsy in the grandparents were selected for this study.

2. Eleven cases presented parents who were normal; that is, patient and grandparents were epileptic while the parents were non-epileptic. In other words, 11 cases or 52% were the offspring of epileptic parents, and were also the parents of epileptic offspring, but did not themselves have epilepsy.

3. Seven of the cases had epileptic children, making seven cases in which epilepsy continued through three generations, or 33⅓% of the 21 cases.

4. Three cases presented migraine in the second generation with epilepsy in the first and third generations, or about 14%.

In our 1000 cases 27 were found with seizures in a grandparent, four of whom gave a positive history of seizures in parents, *i. e.*, four cases with seizures occurring in three successive generations (4 out of 1000). A study of the findings in their parents (representing the middle or second of the three generations) is reported in Section XII, Table VIII.

[4] Since the cases of this nature are so rare, confirmation or denial of this statement is proving to be difficult. However, we have a small number of cases with both parents epileptic (not in the 1000 studied) whose incomplete histories are being brought up-to-date for future study and subsequent presentation.

Kunzi (18) studied 143 children of 62 married epileptics and found an incidence of epilepsy in only 3% (four epileptic children). (Compare with 6.9% of our 87 epileptic parents—Table II).

Kraepelin (16, 17) considers the incidence of inherited epilepsy to be 7.6%. Ostman (30) places it at 4½%, Snell (33) at 11½%, and others vary it from .9% (Weigandt) to 85% (Bolton). Minkowska (25, 26) in 1931 presented the results of a personal study of 1000 persons representing six consecutive generations in two families in Switzerland. Her study began with two individuals labeled F and B. F was the paternal great-great-grandfather, born in 1777, and diagnosed as insane according to a medical certificate. The type of insanity was inferred to be dementia præcox. B, the maternal great-great-grandfather, was born in 1761 and is stated as being a "known epileptic." Of the 1000 persons representing these two family trees, only eight were found to be epileptic, or less than 1%. Ely (10) in a study of 171 persons with "idiopathic epilepsy" found 14% of them showing epilepsy in parents, as compared with 5.7% showing epilepsy in the parents of 104 non-epileptic persons who had migraine. He concludes that ancestral epilepsy is a less important factor in predisposition to epilepsy in the offspring than has previously been believed.

Lennox and Cobb (21) have tabulated the case histories of 1464 extramural patients. Of the 9338 near relatives of these patients 2.6% gave a history of having had seizures. The percentage was 3.5% for parents, 2.8% for siblings, and 1.1% for children. These data are pertinent for comparison with our own because the forms used in the collection of the information were the same as those used by us.

However, both of these authors agree that "in most of the older writings there is far too much emphasis on the inheritance of epilepsy" (4), and that "heredity . . . . is a factor which has been grossly overemphasized" (19).

Patrick and Levy (32) in considering early convulsions in the life histories of 500 epileptics found that they occurred five times as frequently as in the early years of 752 unselected cases.

Burr (3) found an incidence of 2.4% of epilepsy in the parents of 1449 non-institutionalized epileptics. He writes: "My statistics do not show that direct inheritance is important since only 34 parents out of 1449 cases were known to be affected."

Lastly, Myerson (28) states that a hereditary tendency for epilepsy has not been shown. He writes: "There is a curious fact which I have unearthed which bears heavily on the whole problem. If epilepsy is a hereditary disease one would expect it to occur frequently in siblings, that is brothers and sisters. . . . . In my own private and hospital practice, which is extensive, I rarely see brothers and sisters who are epileptic. It does occur, of course, but it is by no manner of means so prominent as feeblemindedness. . . . . At the Waverly School for the Feebleminded there are at the present time 60 families of brothers and sisters numbering 130 individuals . . . . out of a total population of 1500. At Wrentham State School (for feebleminded) there are 80 families of brothers and sisters numbering 300 individuals out of the total population of 1300. . . . . In Taunton State Hospital (psychoses) . . . . there were in 1917 about 160 related persons, mostly brother and sister groups, out of a total population of 1400 . . . . representing about 55 families." Thus, the situation in mental diseases, dementia præcox, manic depressive insanity, and involute psychoses, was not unlike that of feeblemindedness. What is the situation in epilepsy? The superintendent of the Massachusetts State Hospital for Epileptics at Monson (1917) states in reply to a letter there are practically no families of epileptics in the institution numbering 1500 people, and a thorough search revealed four families of 11 people: four as against 60 in one institution, 80 in another, of the feebleminded, and as against 55 in the psychiatric groups. . . . . This one fact is worth more, in my opinion, than a thousand coincidences of migraine, blindness, deafness, etc., in the near and remote ancestors of the epileptics."

We have gone to some length to quote in detail this last statement of Dr. Myerson because our own study does not tally with this impression which we respectfully desire herein to correct. A search of the records, as yet incomplete, has revealed here at Monson the following relation groups: 1—46 brother and sister groups of 95 individuals known to be epileptic, most of whom have been at some time or other patients at Monson. 2—of these, 30 brother and sister groups composed of 64 individuals were found among the 1000 case histories in this survey. 3—They also included 15 pair of twins, 11 pair of which were homologous twins.*[3] 4—18 patients were found with known epileptic parents, most of whom were or had

been in Monson. 5—and 18 more were found with an uncle or aunt having epilepsy; again, mostly in Monson. There were a lesser number of cousins, nieces and nephews, and three with half-siblings with epilepsy. Thus, there have been found, so far, over 80 related groups of more than 170 individuals, 64 of which families were either parent and child or brother and sister groups, as stated, who are known to have had epilepsy, most of them patients at Monson at one time or another during the past 15 or 20 years. These figures are quite comparable to those that Myerson reports for the other institutions; but do not, as far as we can see, prove or disprove anything, except perhaps that epilepsy, like the other neuropsychiatric conditions which he mentions, does not tend to run in families.

Explanation of Table II.—Column A represents the relations of 1000 epileptics as follows: (*1*)—1000 fathers; (*2*)—1000 mothers; (*3*)—average of 2000 total parents; (*4*)—945 of the 1000 epileptics had one or more brothers and sisters (siblings); (*5*)—the total number of siblings was 4305, including 34 half-siblings; (*6*)—87 of the patients had one or more children; (*7*)—the total number of children being 267; (*8*)—represents the patients reporting positive data in any and all relatives other than parents, siblings and children (excluding, of course, in-laws); and these are analyzed further into (*9*)—blood relations, which include the line of direct heredity, viz., grandparent, parents, aunts, uncles, siblings (and 32 half-siblings, as explained in the respective sections), and children, calculated per 1000 patients or families represented; (*10*)—gives the totals for any and all members of the immediate family only, that is, parents, siblings (and the few half-siblings), and children, analyzed per 1000 patients or families represented; and also in (*11*) analyzed for their total number of individual relations which was 6572 parents, siblings and children; (*12*)—represents the positives for any and all relations including all of those mentioned above and the cousins, nieces, nephews, but excluding relations by marriage. These were also calculated per 1000 patients or families to whom they belonged.

Columns B, C, D, E, F, G and H represent respectively the various neuropsychiatric conditions found in the above-mentioned relations, viz., B, seizures, C, migraine, D, feeblemindedness, E, alcoholism, F, psychosis, G, miscellaneous and H, total neuropsychiatric disorders.

TABLE II.

INCIDENCE OF NEUROPSYCHIATRIC DISEASES IN THE FAMILIES OF 1000 EPILEPTICS.

	A	B		C		D		E		F		G		H	
	Relations.	Seizures		Migraine.		F. M.		Alcoholism.		Psychosis.		Miscell.		Total N. P.	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1	Fathers (1000)	23	2.3	19	1.9	5	0.5	222	22.2	12	1.2	86	8.6	316	31.6
2	Mothers (1000)	35	3.5	139	13.9	19	1.9	27	2.7	16	1.6	146	14.6	305	30.5
3	Parents (total) (2000)	58	2.9	158	7.9	24	1.2	249	12.5	28	1.4	232	11.6	621	31.1
4	Patients or families with siblings (945)	117	12.4	28	3.0	66	7.0	21	2.2	19	2.0	72	7.6	275	29.1
5	Total number of siblings (4305)*4	176*5	4.1	33	0.8	92*6	2.1	26	0.6	24	0.6	146	3.4	439*7	10.2
6	Patients with children (87)	6	6.9	1	1.1	6	6.9	1	1.1	0	0	9	10.3	18	20.7
7	Total number of offspring (267)	6	2.2	1	0.4	6	2.2	1	0.4	0	0	18	6.7	23	8.6
8	1000 patients with (any-all) other relatives	132	13.2	40	4.0	8	0.8	57	5.7	40	4.0	136	13.6	226	22.6
9	1000 patients with blood relations*8	236	23.6	193	19.3	67	6.7	254	25.4	67	6.7	310	31.0	617	61.7
10	Immediate family only (parents, siblings and children)	181	18.1	170	17.0	66	6.6	228	22.8	47	4.7	307	30.7	606	60.6
11	Total number of parents, siblings and children (6572)	240	3.7	192	2.9	122	1.9	276	4.2	52	0.8	396	6.0	1098	16.7
12	Any-all relatives of 1000 patients	274	27.4	196	19.6	69	6.9	201	20.1	78	7.8	367	36.7	680	68.0

*4 Includes 34 half-siblings.

*5 Includes 3 half-siblings with seizures.

*6 Includes 2 half-siblings with feeble-mindedness.

7 Includes 5 half-siblings.

8 Includes grandparents, parents, aunts, uncles, siblings and children—per 1000 patients.

The two smaller columns under each of these titles represent, 1st, the number of individuals with positive histories, *i. e.*, relatives, as specified at left in Column A, and 2nd, their percentage, on the basis of either total number of patients or families represented, or total number of relatives, also as specified in Column A.

Study of Seizures—Column B—Table II.—By the term "seizures" is meant any kind of convulsion or fit that occurred one or more times in the life history of the relation of the patient. Nearly a third of these were definitely stated to have been restricted to childhood and were singular rather than plural in number; actually recognized and diagnosed epilepsy was reported in only about one-third of the relatives with seizures.

As seen in Column B, seizures occurred in 23 fathers and 35 mothers, or 1½ times as many mothers as fathers. The total for the parents was 58 out of 2000 or an average of 2.9% of the total parents, but 5.8% of the patients with parents since in no case were seizures reported in both parents. No cases giving a history of seizures in both parents were found in this study. One hundred and seventeen epileptics reported seizures in one or more siblings, three of whom were half-siblings; a figure which is 12.4% of the total number of 945 patients having brothers or sisters. However, the total number of brothers or sisters who had seizures was only 176 out of 4305 siblings or 4.1%. Nevertheless, seizures appear more than twice as frequently in the siblings of the epileptics (12.4%) as in their parents (5.8%) and (if one chooses to use the scant number of 87 cases with children) twice as often in the siblings as in children (6.9%).

Eighty-seven epileptics of both sexes had a total of 267 offspring but only six of them had six children with seizures (one child per family or patient). These figures for offspring are too few in number to be of much value but even so the incidence of seizures in the offspring is decidedly smaller than one might expect.

Seizures occur more frequently in the immediate family (*10*)—Table II—18.1%—than in all the other relations (*8*) (13.2%). But although 18.1% of the patients report a positive history of seizures in some member of the immediate family (*10*) (parents, siblings or children), the actual incidence of seizures in the total 6572 parents, siblings and children (*11*) was only 240 persons or 3.7%.

The total incidence of seizures in any and all relations of the 1000 patients (*12*) was 274 or 27.4%. In other words, slightly more than one-quarter of the epileptics give a positive history for seizures in one or more of any of their relations. These figures are from three to eight times greater than the corresponding groups in the control figures; (*v.* Tables III and IV).*[11]

Explanation of Table III.—As in Table II, Column A represents the relations of 1115 controls and Columns B, C, D, E, F, G and H the neuropsychiatric conditions of seizures, migraine, feeble-mindedness, alcoholism, psychosis, miscellaneous neuropsychiatric and total neuropsychiatric disorders respectively.

One thousand, one hundred and fifteen controls were studied for seizures and migraine.*[2] *[9] This group included (*1*)—1115 fathers, (*2*)—1107 mothers, (*3*)—2222 total parents; (*4*)—997 controls had a total of (*5*)—4381 brothers and sisters; and (*6*)—175 controls had a total of, (*7*)—456 children; (*8*), (*9*), (*10*), (*11*), and (*12*) were calculated for 722 controls composed of the following relations: (*1*)—1444 parents; (*2*)—2925 brothers and sisters (including nine half-siblings) belonging to 644 families; and (*3*)—315 children of 139 controls. Columns D to H represent the data for 722 controls.*[10]

Columns D, E, F, G and H represent the positives respectively in (*1*)—722 fathers, (*2*)—722 mothers, (*3*)—1444 total parents, (*4*)—644 controls had (*5*)—2925 siblings (including nine half-siblings) and (*6*) 139 controls had (*7*)—315 children; 722 controls reported on (*8*)—other relations; (*9*)—blood relations; (*10*)—immediate families only, of whom there were (*11*)—4684 total parents, siblings, and children, and 722 reported on (*12*) any and all relations except relations by marriage. The two smaller columns under each of these titles represent 1st, the number of positives in the relations as specified at the left in Column A, and 2nd, their percentage of the total.

Study of Seizures—Table III.—Seizures were reported in three fathers and five mothers, an average of 0.4% in the total parents. Thirty-one of the controls reported seizures in 35 brothers and sisters, an incidence of 3.1% (*4*) which is eight times greater than in parents, although of the total 4385 siblings (*5*) only 0.8% had

*[11] Analysis of Columns B to H, inclusive, are to be found under the respective headings below, Sections V to X, inclusive.

TABLE III.

Incidence of Neuropsychiatric Diseases in the Families of 1115 Controls. *2, *9, *10

	A	B*9		C*9		No. of Relations.	D*10		E*10		F*10		G*10		H*10	
	Relations.	Seizures.		Migraine.			F. M.		Alcoholism.		Psychosis.		Miscell.		Total N. P.	
		No.	%	No.	%		No.	%	No.	%	No.	%	No.	%	No.	%
1	Fathers (1115)	3	0.3	22	2.0	722	0	0.0	38	5.3	1	0.1	24	3.3	79	10.9
2	Mothers (1107)	5	0.5	93	8.4	722	0	0.0	0	0.0	6	0.8	25	3.5	80	11.1
3	Parents (total) (2222)	8	0.4	115	5.2	1444	0	0.0	38	2.6	7	0.5	49	3.4	159	11.0
4	Controls (families) with siblings (997)	31	3.1	19	1.9	644	1	0.2	21	3.3	4	0.6	23	3.6	88	13.7
5	Total number of siblings (4381)	35	0.8	20	0.5	2925	3	0.1	26	0.9	4	0.1	23	0.8	208	7.1
6	Controls with children (175)	3	1.7	0	0.0	139	0	0.0	0	0.0	0	0.0	2	1.4	5	3.6
7	Total number of offspring (456)	4	0.9	0	0.0	315	0	0.0	0	0.0	0	0.0	2	0.6	6	1.9
8	Controls with any-all other relations	33	3.0	13	1.2*10	722	5	0.7	22	3.0	26	3.6	93	12.9	188	26.0
9	722 controls with blood relations	45	6.2*10	70	9.7*10	722	11	1.5	65	9.0	21	2.9	123	17.0	212	29.4
10	Immediate family only per 722 controls	33	4.6*10	66	9.1*10	722	10	1.4	46	6.4	11	1.5	86	11.9	186	25.8
11	Total number of parents, siblings and children (4684)	59	1.3*10	160	3.4*10	4684	6	0.1	69	1.5	17	0.4	121	2.6	279	6.0
12	Any-all relatives per 722 controls	48	6.6*10	77	10.7*10	722	11	1.5	66	9.1	27	3.7	131	18.1	217	30.1

*9 Seizures and migraine calculated for 1115 controls, except as noted for (9), (10), (11), and (12).
*10 Calculated for 722 controls.

seizures, which is only twice as great as the 0.4% in 2222 parents. Three controls had four children with seizures; 33 reported seizures in other relatives (*8*); and 45 out of 722 controls reported seizures in blood relations (*9*), that is, grandparents, parents, aunts, uncles, siblings and children. Thirty-three of 722 controls (*10*) reported 59 (*11*) members of the total of 4684 parents, siblings *[12] and children, and 48 (*12*) reported seizures in any and all relations, or 6.6%, a figure which is less than one-fifth as great as for the similar groups in the patients.*[12]

Explanation of Table IV.—Table IV represents a combination of the percentages of positives as noted in Tables II and III. The topic headings and relationships (*1*) to (*12*) inclusive are the same as for Tables II and III and the smaller columns under headings B to H inclusive represent, at left, the percentages of positives in relations of the patients, and at right, the percentage of positives in the same relation groups of the controls.

Study of Table IV.—Seizures occur about eight times more frequently in the fathers of the patients (2.3%) than in the controls (0.3%); seven times more frequently in the mothers of the patients (3.5%) than in the controls (0.5%) and four times as often in the siblings of patients (12.4%) as in the siblings of the controls (3.1%) although the incidence of seizures in the total number of siblings (*5*) is five times greater in patients (4.1%) than in the controls (0.8%). In (*8*) seizures occur five times as often in the other relations of the patients (14.2%) as in the other relations of the controls (2.9%) and similar proportions exist for the remaining groups. Seizures occur more than four times as often in all (any) relations of the patients as in all (any) relations of the controls.*[12]

V. Migraine.

Migraine, and its relation to epilepsy, as well as its possible inheritance, either as migraine or as epilepsy, in the offspring of migrainous parents is also a moot question. "The close relationship between the occurrence of epilepsy and the migraine has been noted for many years," write Lennox and Cobb (*20*). "Indeed," they continue, "many authors believe that migraine attacks are but sensory seizures."

*[12] None of the half-siblings reported seizures in the new parent.

TABLE IV.

Relative Percentage Incidence of Neuropsychiatric Diseases in the Families of 1000 Epileptics and 1115 Normal Non-Epileptic Controls (Except as Noted).

Comparison of Tables II and III. *2

	A	B*13		C*13		D*14		E*14		F*14		G*14		H*14	
	Relations.	Seizures.		Migraine.		F. M.		Alcoholism.		Psychosis.		Miscell.		Total N. P.	
		Pts.	Con.	Pts.	Con.	Pts.	Con.	Pts.	Con.	Pts.	Con.	Pts.	Con.	Pts.	Con.
1	Fathers	2.3	0.3	1.9	1.9	0.5	0.0	22.2	5.2	1.2	0.1	8.6	3.3	31.6	10.9
2	Mothers	3.5	0.5	13.9	8.4	1.9	0.0	2.7	0.0	1.6	0.8	14.6	3.4	30.5	11.1
3	Parents (total)	2.9	0.4	7.9	5.2	1.2	0.0	12.5	2.6	1.4	0.5	11.6	3.4	31.1	11.0
4	Individuals or families with siblings	12.4	3.1	2.9	1.9	7.0	0.2	2.2	3.3	2.0	0.6	7.6	3.6	29.1	13.6
5	Total number of siblings	4.1	0.8	0.8	0.5	2.1	0.1	0.6	0.9	0.6	0.1	3.4	0.8	10.2	7.1
6	Individuals with children	6.9	1.7	1.1	0.0	6.9	0.0	1.1	0.0	0.0	0.0	10.3	1.5	20.7	3.6
7	Total number of offspring	2.2	0.9	0.4	0.0	2.2	0.0	0.4	0.0	0.0	0.0	6.7	0.6	8.4	1.9
8	Individuals or families with any-all other relatives	13.2	3.0	4.0	1.8*15	0.8	0.7	5.7	3.0	4.0	3.6	13.6	12.9	22.6	2.6
9	Individuals or families with blood relations	23.6	6.2*15	19.3	9.7*15	6.7	1.5	25.4	9.0	6.7	2.9	31.0	17.0	61.7	29.3
10	Immediate families only	18.1	4.6*15	17.0	9.2*15	6.6	1.4	22.8	6.4	4.7	1.5	30.7	11.9	60.6	25.7
11	Total number of parents, siblings and children	3.6	1.3*15	2.9	3.4*15	1.8	0.1	4.2	1.5	0.8	0.4	6.0	2.6	16.7	5.9
12	Any-all relatives per individual or families	27.4	6.6*15	19.6	10.6*15	6.9	1.4	20.1	9.1	7.8	3.7	36.7	18.1	68.0	30.0

*13 1000 patients and 1115 controls.
*14 1000 patients and 722 controls.
*15 722 controls.

Ely (10) studied 104 migrainous patients, 171 "idiopathic" epileptics and 100 normal persons and concluded—"There is a preponderance of evidence indicating some definite clinical relationship between migraine and epilepsy," and "a migrainous ancestral trend predisposes the offspring to epilepsy." Thom (36) in an earlier paper, thought that the hereditary factors causing migraine and epilepsy were interchangeable and might appear as migraine in a parent and as epilepsy in the offspring, or vice versa. Levy & Patrick (23) are of the opinion that, "parents who fainted or who had periodic headaches were more likely to have children who had infantile convulsions, temper tantrums, and spells of vomiting or fainting." They summarize as follows: "The frequency of periodic headache in groups of apparently normal women in five communities was as high as 40.2% and this percentage is probably lower than the actual frequency. These headaches likely were largely migraine." Burr (3) omits migraine from his study entirely. He writes: "Migraine, one of the commonest of diseases, yet so rarely mentioned that it is not recorded because any conclusions would be fallacious . . . . probably it is such a common ailment that people forget about it." Cobb (4) found an incidence of 4.3% of migraine in 9139 near relatives of 1086 non-traumatic and non-institutional epileptics as compared with 1.4% in the relatives of 235 epileptics who had suffered head trauma and in 1.5% in the 1896 relatives of 250 normal controls. Myerson (28, page 63) finds migraine occurring in only 3% of the mothers of 100 epileptics (compare this with our own figure of 13.9%—Table II, Column C).

Explanation of Column C—Tables II, III and IV.—The term "migraine," as used here, is not strictly the classical hemicrania, with scotomata, nausea, and vasomotor facial changes. Obviously, an accurate report on these would be impossible to expect from the average observer. We have accepted, therefore, any fairly frequent periodic attacks of more or less severe headache, accompanied by nausea or vomiting, and causing some degree of incapacity, usually necessitating bed rest. All other types of headache, if severe, or incapacitating, or periodic, are classed with the miscellaneous neuropsychiatric conditions in Column G.

In Column C of Table II one is confronted with a relatively high incidence of migraine in mothers (13.9%) as compared with 1.9% for fathers and with 3% for siblings. As seen in Tables III

and IV, however, (Column C) there is a corresponding ratio in the controls. The high figure for (*10*) members of the immediate family is due to this high incidence in the mothers and the danger of judgment from statistical averages is nicely demonstrable at this point; thus, the *average* incidence of migraine in parents is given as 7.9% (*3*) (Table II) which is correct enough since 19 fathers plus 139 mothers, total 158 parents, out of the 2000. Yet, actually, migraine appeared in less than 2% of the fathers and in nearly 14% of the mothers, or seven times as frequently in the mothers as in the fathers. A similar apparent discrepancy appears under alcoholism (Column E—Table II) and with the average of the ages on admission and the ages of onset of seizures.*

In Table IV (Column C) it will be observed that the difference between the incidence of migraine in patients and controls is much less marked than is that for seizures, being only one to four times greater in most instances of the patients than in the controls. Two exceptions are noted; namely, in (*1*) fathers, where the incidence is the same (1.9%) and in (*11*) where the incidence for the total members for the immediate families is greater in the controls (3.4%) than in the patients (2.9%).

Forty-two controls reported migraine in themselves, and were not classed with the positives for siblings. If these 42 controls are classed with positives in siblings then the total for siblings in the controls (Column C—Tables III and IV) should read 62 in 55 families or 1.4% of the total siblings in 7.6% of the controls. Before drawing conclusions on these figures it is well to recall the statement of Burr (3) above—viz., that migraine is probably such a common ailment that people forget about it.

VI. Other Neuropsychiatric Diseases.

In reviewing the literature on the relationship between epilepsy and other neuropsychiatric diseases, one finds included under the latter title a large and heterogeneous grouping of such items as "criminality, blindness, deformity, goiter, vagrancy," (7), "alcoholism, feeblemindedness, insanity," (37), and many others, such as "extreme nervousness, sexual immorality, and lack of moral sense" (11), as well as the usual organic disorders listed in the standard texts of neurology and psychiatry.

In our own study, four groups stand out, not only from the viewpoint of frequency in occurrence, but also as being more consistent with the general impression of what most writers consider to be the conditions that are most frequently met with in so-called "neuropathic taints," "predisposing factors," "hereditary tendencies," or whatever one may choose to call them. These four groups are:

1. Feeblemindedness, long believed to occur in hereditary proportions.
2. Alcoholism, in all degrees from "moderation" to "intoxication," according to personal opinion.
3. Psychoses, other than those listed under epilepsy, feeblemindedness and alcoholism.
4. A large miscellaneous group including organic, emotional, social and behavior manifestations, many of which are neither neuropsychiatric *per se* nor hereditary in character.

VII. Feeblemindedness.

This condition is placed first in our consideration for two reasons: first because it is a disease that has long been recognized as occurring in proportions that suggest a hereditary nature, and secondly because it is so frequently found associated with epilepsy. Here at Monson, for example, about 50% of our admissions fall quite definitely into the feebleminded class. However, deterioration, characteristic of epileptics, doubtless contributes largely to this high percentage, and must not be confused with primary feeblemindedness. In fact, feeblemindedness *per se* is reported as an assigned etiological factor in only 0.6% of our 1000 cases. The not infrequent examples of a number of members of the same family having one or the other of the two diseases—that is, feeblemindedness or epilepsy, lends much weight to the opinion of Yakovlev and Guthrie (39) that a definite embryological basis does exist for the two diseases. They believe that malformation of the primitive ectoderm results in defective integration of nervous functions, a condition which is frequently associated with mental deficiency; and that it is this factor which affords frequent examples of hereditary predisposition which may eventuate in the chronic convulsive state known as epilepsy.

Calling attention to the large group of organic causes of feeblemindedness and to the various classifications where known causes exist, *e. g.*, in cretinism, syphilis, etc., Myerson (28, page 83) points out that nevertheless feeblemindedness does occur in much too large

a portion of the ancestors to be accidental. He writes: "We have, then, the undoubted fact that some forms of feeblemindedness tend to run in families, but we still have as unknown the explanation of its origin since we see it arise *de novo* in normal groups . . . . and become familial. . . . . Further, like mental disease of other types, it tends to become extinct. Kunzi (18) found five feebleminded among his 132 children of 62 epileptics, or 3.8%, while Minkowska (26) remarks on only two feebleminded in one family in her 1000 relations, a figure which is probably incomplete.

Our own incidence at Monson (Table II—Column D) was 1.2% for parents, 7.0% for siblings, and 6.9% for children per patient; but 2.1% (5) for the total of 4305 siblings and 2.2% for the total of 267 children.

Study of feeblemindedness (Column D)—Tables II, III, and IV.—Feeblemindedness occurs in much smaller proportions in the families of epileptics than do seizures and migraine; thus, only five fathers, 19 mothers and 92 brothers and sisters (including two half-siblings) were reported as feeble-minded. However, these 92 siblings belonged to 66 patients; that is, represented 66 families, or 7%, a figure which is 35 times greater than that for the controls (0.2%) (4)—Table III and IV. Feeblemindedness occurs about one-half as frequently as do seizures in the parents and siblings of the epileptics, but just as frequently as seizures in the children (6.9%) (6). Feeblemindedness also occurs nearly six times as frequently in siblings per family (7.0%) as in parents (1.2%), although of the total number of 4305 siblings only 92, or 2.1%, were feebleminded. (5)—Column D, Tables II and IV.

Of the 1000 epileptics 66, or 6.6%, reported feeblemindedness in parents, siblings or children, (10)—Table II—Column D, but of the total number of 6572 parents, siblings and children (11) Table II—Column D, only 122 or 1.9% were feebleminded (the 122 parents, siblings and children belonged to 66 families or patients).

VIII. Alcoholism.

Alcoholism, long blamed for human ills, may also be disputed as being a neuropsychiatric disease. Whether or not it is an evidence of an unstable or psychopathically inferior make-up is beyond the province of this paper to discuss. It must be pointed out, however,

that only a small percentage of those reporting alcoholism reported anything like excessive alcoholic intoxication; and that many (the majority) who did report "moderate alcoholism" might properly be questioned as to just what does constitute moderation. For, as Burr (3) points out: "The degree of alcoholism varies with the examiner's opinion and that of the relatives as to whether it is moderate or excessive."

Myerson (28—page 63), commenting on Binswanger's investigation (1) finds epilepsy as common in non-drinking peoples as in drinking peoples, but agrees that injury to the germ plasm from toxic causes is more likely to be productive of epilepsy than is heredity. "What needs emphasis," writes Dr. Myerson (28—page 42), "is . . . . that germ plasms are not all alike in their resistance to toxins, any more than other tissues are." "Thus, ... one man may get drunk on a glass of whiskey while another drinks a quart without definite or noticeable injury, just as some are poisoned by fish, or this or that protein, which to the majority are forms of nourishment. The wide variability of the human being is an outstanding factor in all discussions on human problems, and it does not seem improbable that this extends to the resistance of the germ plasm."

Burr found 155 fathers, two mothers and eight both parents as alcoholics in his study of 1449 cases of non-institutionalized epileptics. Spratling (34) found alcoholism appearing in the antecedents of 14% of epileptics. Other estimates vary considerably. Stucklich and Gowers (12) place it at 40%; Lewis and Hubbard (22) at 10% in the parents of 160 negro epileptics, while Boven estimates it at 61%, and Redlich at 4.2% of 214 epileptics. For our own findings on alcoholism we return to a study of Column E in Tables II, III, and IV (Section IV).

Study of Alcoholism (Column E)—Tables II, III and IV.—As in migraine, the figures do not tell the entire story, for the *average* incidence of alcoholism for parents (3) (Table II) is 12.5% whereas it actually appears 8.5 times as frequently in the fathers (22.2%) as in the mothers (2.7%).

In contrast with Seizures (Column B), alcoholism appears more than five times as frequently in the parents (3) (Column E) (12.5%) as in the siblings (4) (2.2%) and in only one of the 267 children (7) (0.4%).

The high figure in the other relation groups (*9*), (*10*), (*11*) and (*12*) is largely due to the high incidence in fathers, since in relatives outside of the immediate family (*8*) the incidence of alcoholism is only 5.7%. It is necessary to carefully study and fully appreciate these figures before drawing conclusions on the comparable incidences of alcoholism 20.1%, migraine 19.6%, and seizures 27.4% in any and all relations (*12*) of the 1000 patients. Nevertheless, with but one exception the figures for alcoholism are consistently higher in the epileptic families than in the controls (Column E, Table IV), the exception being for siblings (*4*) and (*5*) in whom alcoholism appears to a higher degree in the controls (3.3%) than in the patients (2.2%).

In the control group (Column E, Tables III and IV) alcoholism appears twice as often in fathers (*1*) as in siblings (*4*), and not at all in mothers (*2*) or children (*6*). The incidence of alcoholism in all relations (*12*) is more than twice as great in the patients (20.1%) as in the controls (9.1%).

The graphic curves showing the relative incidence of seizures, migraine, feeblemindedness, and alcoholism in the families of the epileptic groups are presented in Fig. I, *q. v.*, below.

ALCOHOLISM AT TIME OF CONCEPTION.

Alcoholism at the time of conception was reported in 12 cases in the epileptic group but probably occurred to a much higher extent, considering the relatively high percentage of alcoholism admitted in the fathers. It was not asked for in the control group.

Explanation of Fig. 1.—The curves, reading from above down at left represent respectively: *A*—alcoholism (heavy broken line); *S*—seizures (solid line); *M*—Migraine (dotted line); and *F. M.*—feeblemindedness (alternating dashes and dots).

The ordinates are in percentage from 1-30; and the abscissæ from (*1*) to (*5*) read as follows: (*1*) Fathers (1000); (*2*) mothers (1000); (*3*) siblings—of 1000 patients (or families represented); (*4*) immediate families, *i. e.*, of 1000 patients reporting a positive history for seizures, migraine, feeblemindedness and alcoholism in any member of the immediate family (parents, siblings or children) (*5*) represents the percentage of positives in the total of 6572 parents, siblings and children.

Comment on Fig. 1—It will be observed that the curves for seizures (S), migraine (M), and feeblemindedness (F.M.) all begin low, under 3%, in fathers (*1*); that seizures and feeblemindedness rise slightly but proportionately in mothers (*2*) and diverge while rising in siblings. They rise in (*4*) since this represents the proportion of patients reporting positive histories for these conditions in some member of their immediate family; while in (*5*), representing the percentage of positives in the total members of the immediate family, all four curves descend to a low level

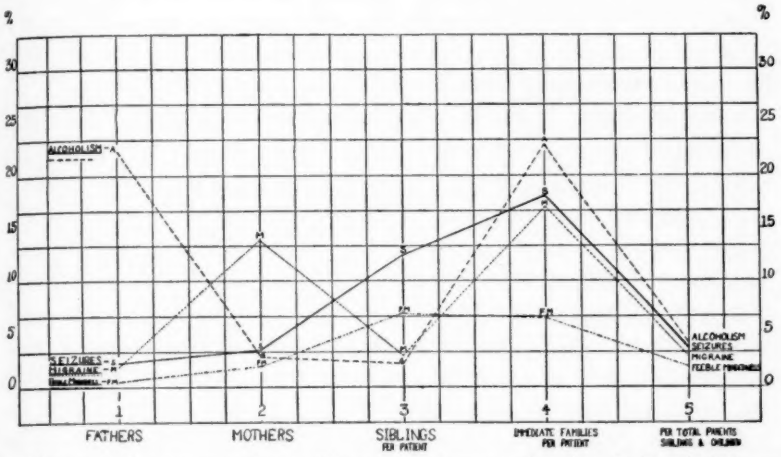

FIG. 1.—The comparative incidence of seizures, migraine, feeblemindedness and alcoholism in the families of 1000 epileptics. Enlarged to 3 times natural scale.

only slightly higher, excepting alcoholism, than that for fathers only.

The curve for alcoholism is conspicuous for its high incidence in fathers (*1*) which is responsible for the high mark in immediate families (4); while the curve for migraine, being highest in mothers, takes a similar high turn in (*4*). Both alcoholism and migraine are conspicuously low for siblings (*3*) and feeblemindedness remains generally low throughout.

The curve for psychoses is not represented here because it is restricted to exclude those of feeblemindedness, alcoholism and epilepsy. It would occupy a position similar to, but lower than, that for feeblemindedness.

It is to be remembered that the small percentages among the total members of the immediate families (5) are divided among a larger group of patients, hence the naturally higher curves in (4).

IX. Psychosis.

Under this title is included the types of mental disorders in the relatives excepting those of mental deficiency, alcoholism, and epilepsy, and those listed in the miscellaneous group, *q. v.* below. For this reason the incidence of psychosis (schizophrenia, manic depressive, involutional melancholia, etc.) in the immediate families is rather low. Little is found in the literature on the relationship between psychosis in general and epilepsy in particular. Myerson has some interesting comments in his book "The Heredity of Mental Diseases" (28) on the tendency for mental diseases to be self-limited and not to run over three generations. In fact, he is of the opinion that some forms of mental deficiency and manic depressive psychosis (and to some extent præcox and the paranoid psychosis) seem to be the only diseases that do run in families of one, two or three generations and in siblings but to go no further. Our own findings would seem to fall in line with these impressions, since to date only 27 cases reported seizures in a patient and in a grandparent, and of these only seven give a history of seizures in the three generations (see Section 4).

Study of Psychosis (Column F) in Tables II, III and IV.—The incidence of psychosis (Tables II and IV) in the relatives of our 1000 epileptics is low in comparison with that for seizures, migraine and alcoholism; but still is from 2 to 12 times more frequent in the same groups (1) to (7)—immediate families of the controls (Tables III and IV). However, psychoses are reported in nearly the same proportion in the other relatives (8) outside of the immediate families of the controls (3.6%) as of the patients (4.0%).

The incidence of psychosis for any or all relations (12), however, is more than twice as high in the epileptic group (7.8%) as in the control group (3.7%).*[16] In Tables II and IV Column F, it will be

[16] These figures are computed for 1000 epileptics and 722 controls, which is a much higher group than the original 612 patients and 190 controls as first reported and, I think, explains Dr. Pollock's objection (discussion) while at the same time substantiating his contention that they did not meet the ordinary estimates on the incidence of psychoses in the community at large. It also verifies the opinion of Myerson that estimates on less than 500 cases are too likely to be erroneous and therefore of little or no value.

noticed that psychoses occur more frequently in the siblings of patients (*4*) (2%) than in the parents (*3*) (1.4%) and slightly more frequently in the immediate families (*10*) (4.7%) than in the other relatives (*8*) (4.0%).

In the control group (Column F, Tables III and IV) psychoses occur more frequently in mothers (*2*) (0.8%) than in the siblings (*4*) (0.6%) and over twice as frequently in the other relatives (*8*) (3.6%) as in the immediate family (*10*) (1.5%).

The total incidence of psychosis (*12*) in all relations of the patient (7.8%) is about twice as great as in all relations of the controls (3.7%).

X. Miscellaneous Neuropsychiatric Disorders.

This is a large and heterogeneous group of conditions, many of which will be properly questioned as being of neuropsychiatric origin, or for that matter as even being diseases, since a number of them are purely social and economic in origin. Others have definitely known organic causes that have anything but a hereditary character; while still others are essentially emotional and personal in nature. They are listed only for the sake of completeness and to indicate their relative values when compared with the incidences of seizures, migraine, feeblemindedness, alcoholism and psychosis. Obviously, all of the cases of "very nervous," and immoral relations were not reported, either by patients or controls; however, it is probably fair to assume that no greater proportion of these items was forgotten than of seizures, migraine, etc. Following is a list of the miscellaneous neuropsychiatric conditions recorded during the study: chorea, shock, apoplexy, hemiplegia, paralysis, Parkinsonianism, anterior poliomyelitis, neuritis, brain tumor, congenital blindness, nervousness ("very nervous"), nervous breakdown, hysteria, queerness, dullness, or retardation (not included in the feebleminded group), dizzy spells, fainting spells, severe headache, speech defect, tic, habit spasms, attempted suicide, emotional instability, degeneration, perversion, highstrung, desertion, brutality, immorality, vagrancy, and court records for various types of felonies or misdemeanors, including violation of liquor, automobile, and other prohibitory statutes.

The results of a study of these miscellaneous conditions are summarized in Table V; and a more detailed analysis of smaller numbers of them are listed in Tables VI and VII.

Explanation of Table V.—Table V presents the summary of the miscellaneous neuropsychiatric conditions as listed above, and as presented in greater detail below in Tables VI and VII. The numbers are the positives in 381 epileptics reporting miscellaneous neuropsychiatric conditions in 675 (any) relations; and in 131 controls reporting positives for the same data in 145 relations. Obviously the comparison is unfair because of the smaller numbers. The percentages are for the total number of positives in the relations, *i. e.*, in 675 and 145 respectively.

TABLE V.

SUMMARY OF MISCELLANEOUS NEUROPSYCHIATRIC DISORDERS IN 675 RELATIONS OF 381 EPILEPTICS AND IN 145 RELATIONS OF 131 CONTROLS.

Miscellaneous neuropsychiatric conditions.	Patients.		Controls.	
	No. of relations.	%	relations.	%
A—Organic nervous diseases.....	191	28.6	61	42.1
B—Hysteria, nervous breakdown, or "very nervous".....	109	16.1	36	24.8
C—Miscellaneous (other than above)	375	55.5	48	33.1

A partial analysis of the miscellaneous neuropsychiatric conditions reported in 206 families of the first 612 patients, totaling 364 relations, is presented in Table VI.

Explanation of Table VI.—Of 612 epileptics (the first group in the 1000 series) 206 patients reported positive miscellaneous neuropsychiatric diseases in 364 relations, as listed above. No percentages or further calculations were made on this group concerning miscellaneous neuropsychiatric disorders excepting the data presented below in Table VII.

Explanation of Table VII.—This table is self-explanatory. The numbers were too few for worthwhile percentage calculations; and a more extensive study of the miscellaneous neuropsychiatric conditions was not considered necessary for this paper.

TABLE VI.

PARTIAL ANALYSIS OF MISCELLANEOUS NEUROPSYCHIATRIC DISEASES IN 364 RELATIONS OF 206 FAMILIES OF 612 EPILEPTICS.

Miscellaneous neuropsychiatric disorders.	Relations.	Total.
A—Organic	16 fathers; 23 mothers; 29 siblings; 1 child; and 3 other relatives.	72
B—Nervous breakdown, hysteria, or "very nervous".	9 fathers; 27 mothers; 11 brothers and sisters; no children; and 2 other relatives.	49
C—Miscellaneous (other than the above).	57 fathers; 78 mothers; 88 siblings; 11 half-siblings; no children and 9 other relatives.	243
Total miscellaneous neuropsychiatric disorders.		364

TABLE VII.

ANALYSIS OF MISCELLANEOUS NEUROPSYCHIATRIC CONDITIONS AS REPORTED IN 311 (ANY) RELATIONS IN THE EPILEPTIC FAMILIES.

Neuropsychiatric condition.	No. of relations.
1. Shock, stroke or hemiplegia	47
2. Paralysis (any type, including anter. polio)	23
3. Meningitis	17
4. Chorea	8
5. Fainting spells	27
6. Brain fever	6
7. "Water on the brain"	3
8. Neuritis	4
9. Severe headaches (periodic) other than migraine	3
10. Locomotor ataxia	3
11. Encephalitis	3
12. "Spinal trouble"	2
13. Dullness or mental retardation	25
14. "Peculiar," "queer," "unstable"	13
15. Shiftless, brutal, abusive, and desertion	17
16. Immorality or court record	30
17. Suicide	10
18. Tic, habit spasm or speech defect	5
19. Behavior problems or delinquency	3
20. "Mental trouble"	2
21. "Very nervous," nervous breakdown, "emotionally unstable," etc.	60
Total	311

XI. Total Neuropsychiatric.

Column H in Tables II, III and IV represents the total number of individuals, patients and controls respectively, with positives for any and all neuropsychiatric conditions as enumerated in Columns B to G inclusively according to the relationship, as in Column A.

Since a large proportion of these (33% to 50%) are made up of the miscellaneous grouping in Column G, no conclusions are drawn. Like the former group (Column G) the totals are also given solely for the sake of completeness. Figs. 2 and 3 present graphically the

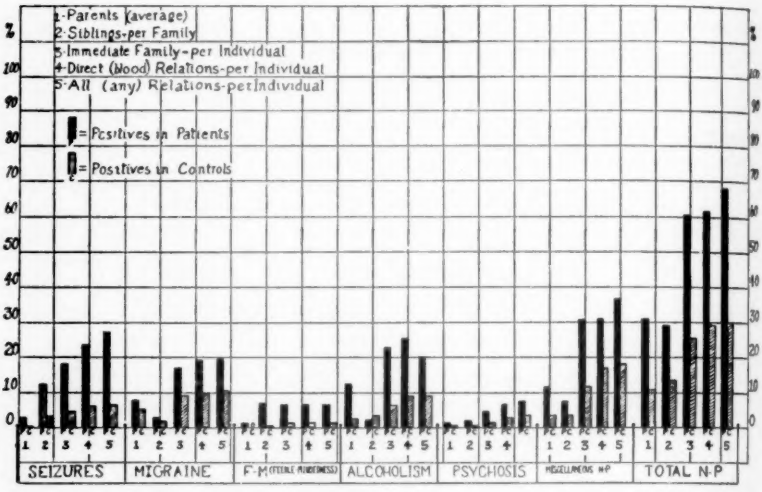

Fig. 2.—The relative incidence of seizures, migraine, feeblemindedness, alcoholism, psychosis, miscellaneous and total neuropsychiatric disorders in the families of patients and controls.

relative incidences of these various neuropsychiatric conditions in the families of both the patients and the controls, as given numerically in Table IV.

Explanation of Fig. 2.—The ordinates are in percentage drawn to correct scale from 1 to 100. The abscissæ represent the respective neuropsychiatric conditions of seizures, migraine, etc., as labelled. The columns are paired. The solid black column P represents the positive histories in patients and the striped column C represents the comparative percentage of positives in a similar group of controls. (Same figures as in Table IV, *viz.*, 1000 patients and 1115 or 722 controls).

The columns are grouped in sets of five for each condition and represent the following relations: 1. Ave. of total parents; 2. Brothers and sisters per individual or family represented; 3. Any (all) members of the immediate family only (parents, siblings or children) per individual or family represented; 4. Any (all) direct blood relations only (grandparents, parents, aunts, uncles, siblings or children) per individual or family represented; and 5. Any (all) relatives per individual or family represented. (Figs. 2 and 3 represent a graphic illustration of Table IV).

Comment on Fig. 2.—With one exception, viz., alcoholism in siblings (2) the positive incidences for all relations of the patients represented by the solid black columns P are conspicuously higher than in the controls—which is in accordance with the figures of Table III. They rise, naturally from left to right since a large number of relations are included.

Column 5 in alcoholism is lower than 4 because of duplication of relations in the same families; since 5 represents the percentage of patients in families reporting positives in all (any) relations.

The formidably tall columns for total neuropsychiatric conditions are shorn of much of their apparent significance when one considers that close to one-half of the total neuropsychiatric disorders is composed of the miscellaneous group of neuropsychiatric conditions enumerated in Table VI, *q. v.*, Section X.

Explanation of Fig. 3.—The ordinates are in percent drawn to three times natural scale. The abscissæ represent the respective neuropsychiatric conditions of seizures, migraine, etc., as labelled. The columns are paired; the solid black column P represents the positive histories in patients and the striped column C represents the comparative percentage of positives in a similar group of controls. (Same figures as in Table IV, viz., 1000 patients and 1115 or 722 controls).

The columns are grouped in sets of five for each condition and represent the following relations: 1. Total Fathers; 2. Total Mothers; 3. Total Siblings; 4. Total Children; 5. Total Parents, Siblings and Children. The percentage of positives are calculated for the totals of each relation group instead of for the patients or families represented as in Fig. 2. (Figs. 2 and 3 represent a graphic illustration of Table IV).

Comment on Fig. 3.—Several things stand out prominently in Fig. 3. Migraine in fathers is equal in patients and controls—and has nearly two-thirds as high an incidence in the mothers of the controls as in the mothers of the patients. Interestingly enough, although Column 5 in Fig. 2 shows migraine higher in all the relations of the patients than of controls—it is higher in proportion to the total number of parents, siblings and children of the controls, than in the same group of the patients (Column 5, Fig. 3). The

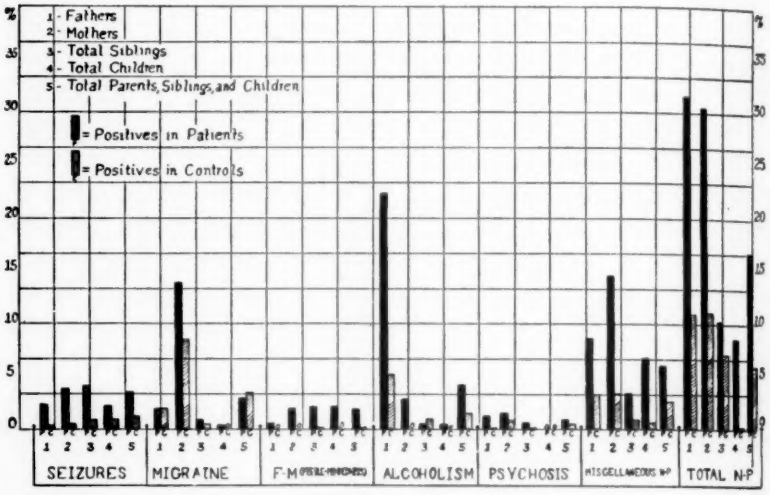

FIG. 3.—The relative incidence of seizures, migraine, feeblemindedness, alcoholism, psychosis, miscellaneous and total neuropsychiatric conditions in the families of patients and controls.

high point for alcoholism in fathers naturally stands out as indicated numerically (Fig. 1 and Tables II and IV) while the high columns of total neuropsychiatric disorders are also due in part to the miscellaneous group; but even so, still reach no higher than one-third of the total fathers and mothers, one-tenth of the total brothers and sisters, one-twelfth of the total children, and less than one-seventh of all the parents, siblings and children. The corresponding figures for the controls, are, of course, considerably smaller as indicated in the striped bars and discussed elsewhere (Table IV).

XII. 27 Cases of Three Generations with Seizures.

Twenty-seven out of our 1000 cases were found giving a positive history of seizures in a grandparent and since the parental history was known this made three generations for study. Table VIII gives an account of the findings in the remaining members of the families in these 27 cases.

Explanation of Table VIII.—Column A represents the relations of the 27 epileptics as follows: 108 grandparents, 27 fathers, 27 mothers, 19 patients with brothers and sisters totaling 110 siblings

TABLE VIII.

Résumé of 27 Cases With Seizures in Patient and in Grandparent.

Relation.	Seizures.	Migraine.	F. M.	Alcoholism.	Psychosis.	Miscell. N. P.
Grandparents (108)	27	0	0	1	1*[17]	0
Fathers (27)	2	0	0	8	0	4
Mothers (27)	2	5	1	0	3	2
Nineteen patients with siblings	4	1	9	0	2	5
Total siblings (110)	4	1	19	0	2	5
Three patients with children	0	0	0	0	0	0
Total children (7)	0	0	0	0	0	0
Aunts and uncles	9	0	0	1	1	0
Cousins	0	0	0	0	1	0

*[17] In a great-grandparent

(including one half-sibling), three patients with offspring totaling seven children, and lastly aunts, uncles and cousins.

Columns B, C, D, E, F, and G represent the neuropsychiatric conditions of seizures, migraine, feeblemindedness, alcoholism, psychosis, and other neuropsychiatric disorders.

Reading from left to right, therefore, 27 of the 108 grandparents reported seizures, one reported alcoholism, and one great-grandparent had a psychosis. Two fathers and two mothers had seizures, five mothers reported migraine, one mother was feebleminded, eight fathers were alcoholic, three mothers had psychoses, and four fathers and two mothers had some miscellaneous neuropsychiatric condition. Four patients out of the 19 with siblings had

three siblings and one half-sibling with seizures out of a total of 110 siblings. One sibling had migraine, 19 siblings belonging to nine families were feebleminded, two had psychoses, and five had miscellaneous neuropsychiatric conditions.

Comment.—None of the seven children of the three patients with offspring had any neuropsychiatric condition at all. In fact, in these three cases the rest of the family history was absolutely free (four generations for study).

Nine patients reported an aunt or uncle with seizures, one with alcoholism and one with psychosis, and one reported a cousin with a psychosis.

The above table represents the rest of the family history in 27 cases having seizures in both the patient and the grandparent. A much larger number of cases will be needed before hastily drawing conclusions from the high incidence of feeblemindedness in siblings. It is hoped to ultimately increase this to a study of a larger number of cases. However, as seen, seizures appear in only four parents, which represents 16.8% of the 27 cases in which seizures appeared in three consecutive generations, as compared with Thom's 33⅓% in 21 cases (34).

This represents an incidence of 4.6% in the immediate family as compared with 3.7% for the whole group.

Obviously, no sweeping conclusions can be drawn from such scanty figures but adding Thom's 21 cases to our 27 we have a total of 48 cases of which 11 present seizures in three generations, or 23%, a figure which tallies with our findings for the appearance of seizures in the average of all blood relatives (9—Table I). The only other high figure is for nine aunts and uncles with seizures representing 33⅓%.

Explanation of Fig. 4.—The ordinates are in percent drawn to correct scale. The abscissæ represent from one to seven inclusively, the various neuropsychiatric conditions enumerated above: viz., 1. Seizures; 2. Migraine; 3. Feeblemindedness; 4. Alcoholism; 5. Psychosis; 6. Miscellaneous Neuropsychiatric; 7. Total Neuropsychiatric Disorders.

The solid black columns with the minus sign beneath represent the negative histories; and the striped columns with the plus sign beneath are the positive histories in A and B respectively.

Each neuropsychiatric disorder is presented for two analyses: A—for the percentage of 1000 patients or families represented; and B—for the total number of 6572 parents, siblings and children belonging to these 1000 patients.

Comment on Fig. 4.—Two impressions are intended to be portrayed in this figure: the first is the extreme disproportion between the low positive and high negative percentage incidence of the various neuropsychiatric conditions throughout, excepting total neuropsychiatric which will be discussed presently.

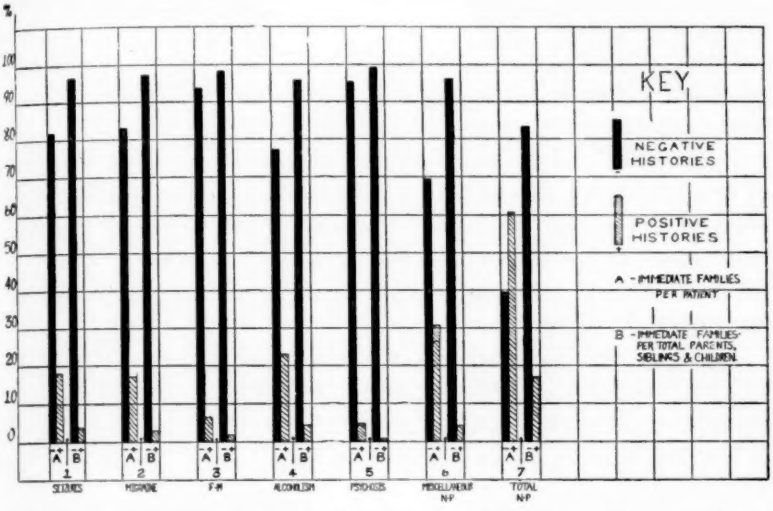

FIG. 4.—The comparative incidence of negative and positive histories of seizures, migraine, feeblemindedness, alcoholism, psychosis, and miscellaneous and total neuropsychiatric disorders in the immediate families of 1000 epileptics.

The second observation is that when these positive percentage incidences are analyzed for the total number of parents, siblings and children as in B—instead of per patient or family represented, as in A—the disproportion is considerably greater—and even the total neuropsychiatric conditions—7—B assume the same constant relative proportion.

Concerning 7-A, it is probably fair to assume that if *all* of the cases of nervousness, immorality, and court records in the families of our patients (as also of the controls) were actually known, the percentage of positive histories for total neuropsychiatric (shaded

column) would be considerably higher than that which is given. Likewise, if all of the infantile fevers and childhood illnesses were correctly diagnosed and recalled for the historian, we might have a different story to tell concerning the etiological factors in epilepsy.

For the purposes of this study one can perhaps gain a fairer impression by either omitting the total neuropsychiatric or deducting therefrom the miscellaneous neuropsychiatric disorders and considering the remaining neuropsychiatric data as presented.

As stated elsewhere, the miscellaneous neuropsychiatric data are included in this study essentially for the sake of completeness in this impartial survey.

In Fig. 5 is expressed still more graphically the relation between positive and negative histories for seizures in the immediate families of patients and controls.

Explanation of Fig. 5—As in Fig. 4, A—represents the analysis of seizures in any member of the immediate family (parents, siblings, children) per individual (patient or control) family while B—represents the analysis of the same data per total number of parents, siblings and children (6572 for the patients and 4684 for the controls).

The circles at the left represent the data for patients. The solid black portion indicates the negative histories while the white parts are the positive histories for seizures.

The circles on the right continue the same arrangement but represent the controls.

Comment on Fig. 5—Fig. 5 presents what the writer considers to be the most important data in this study of heredity in epilepsy. The positive incidences of seizures (white) are here given their true proportions, and deserve careful scrutiny before concluding.

Thus, in A (Fig. 5) the positive incidences of seizures in the immediate families of 1000 epileptics (18.1%) is nearly four times as great as that (4.6%) for the 722 controls. And in B—the percentage of the total number of 6572 parents, siblings and children (3.7%) of the patients is nearly three times as great as (1.3%) in the 4684 parents, siblings and children of the controls.

But, on the other hand, in A—81.9% of the patients show no history of seizures in their immediate family and in B—96.3% of these 6572 parents, siblings and children likewise show a negative history of seizures.

Comparable figures could be made for most of the other neuropsychiatric conditions from the tables given.

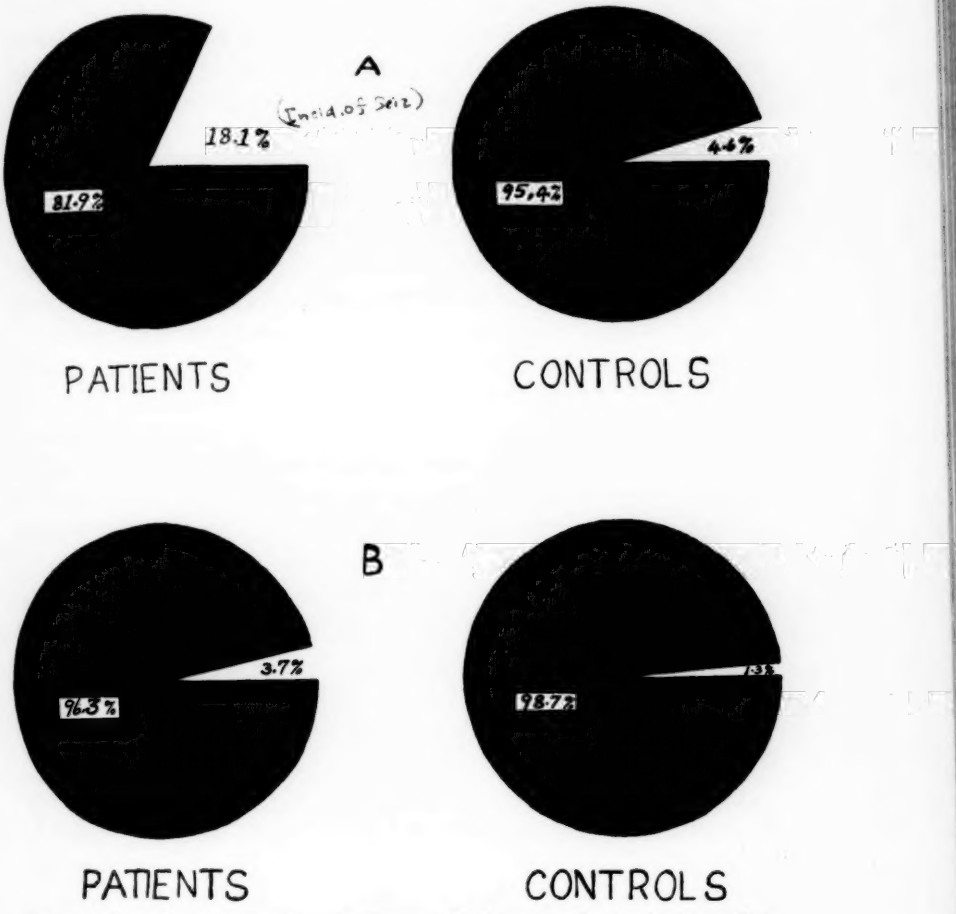

FIG. 5.—Negative and Positive incidence of seizures only in the immediate families of 1000 epileptics and 722 controls.

SUMMARY OF FINDINGS.

1. One thousand complete case histories from the active files of the Monson State Hospital for epileptics in Massachusetts were studied for the incidence of seizures, migraine, feeblemindedness,

alcoholism, psychosis and other neuropsychiatric diseases in the parents, siblings, children and other relatives.

Similar family history records of a control group of 1115 non-epileptic individuals were tabulated for the comparative incidence of seizures and migraine in the same relation groups; and 722 of these were studied for the incidence of the other neuropsychiatric disorders enumerated above.*[a]

Details of the sources of data and methods of collecting same are given in the introduction, Section I.

2. Of the 1000 patients, 486 were males and 514 were females. Nine hundred and forty-five had brothers or sisters (siblings), and 55 were only children. One hundred and eighteen were married and 87 had children. The total number of siblings was 4305, including 34 half-siblings, and the total number of children was 267. The total number of parents, siblings and children was 6572.

Of the 1115 controls, there were 427 males, 672 females and 16 with sex unstated. Three hundred and twenty-four were married, 175 of whom had 456 children. Nine hundred and ninety-seven had siblings, totaling 4381 brothers and sisters. The total number of parents, siblings and children was 5959.

Of the 722 controls, 205 were males and 501 were females, and there were 16 with sex unstated. Six hundred and forty-four had siblings, totaling 2925 brothers and sisters, including nine half-siblings. Two hundred and sixty-seven were married and 139 of them were the parents of 315 offspring. The total number of parents, siblings and children was 4684.

The histories, while presenting the usual elements of human forgetfulness, misrepresentation, and often inadequacy, were taken by the admitting physician from parents or guardian and supplemented by the psychiatric social workers from other sources.

The cases represent a fair cross-section of society in Massachusetts; and all ages and both sexes are represented. The same is true for the controls. The differences between institutional and extra-mural patients do not, apparently, influence the heredity in the respective groups (Section II).

3. The incidence of epilepsy, though varying with authorities, seems to average about 1 in 350 of the general population or about 0.3%.

4. *Heredity in Epilepsy.*—The term "seizure" was selected to represent one or more convulsions or fits in the life history of the individual (relation) up to the time of taking the history. About one-third of those reporting positive histories for seizures in a relative reported only one or two isolated convulsions—usually in infancy or childhood; and about an additional third reported actual epilepsy in the relatives. The literature is reviewed.

5. *Seizures.*—Seizures (Section IV) were reported as occurring in one or more members of the immediate family, that is, parents, brothers and sisters, or children, by 18.1% of 1000 epileptics. This was nearly four times greater than the incidence for a comparable group of controls (which was 4.6%).

On the other hand, of the total 6572 parents, siblings and children, belonging to the epileptic group, only 240 individuals or 3.7% were reported as having had seizures. This was still nearly three times greater than in the corresponding group of controls; viz., 1.3% of 4684 parents, siblings and children of 722 controls.*[3]

In other words, 18.1% of the 1000 patients reported seizures in one or more of their 6572 parents, siblings and children; the proportion of positives to the total of 6572 being 3.7%. Differently stated, however, (Figs. 4 and 5), 81.9% or 819 patients gave no history of seizures in any parents, siblings and children, and 96.3% of their 6572 parents, siblings and children were free from seizures.

Twenty-seven cases with seizures in both patient and a grandparent were studied for the rest of their family history. (Table 8, Section XII). This group was considered too small for any worthwhile conclusions. However, four of the cases presented a history of seizures in a parent also; and four of them reported seizures in siblings. Eight had alcoholic fathers and nine had feebleminded siblings. Three of them had seven children (all normal) making four generations accounted for. Thom's 21 cases are compared.

6. *Migraine.*—Migraine (Section V) was reported as occurring most frequently in the mothers of both patients (13.9%) and controls (8.4%). No particular relationship was noted between migraine and seizures. The incidence for the immediate family was nearly twice as high per individual, *viz.*, 17.0% of the patients and 9.2% of the controls, but actually the incidence of migraine was

greater in the relations of the controls (3.4% of the total parents, siblings and children) than in the immediate family of the patients (2.9%).

7. *Feeblemindedness.*—Feeblemindedness (Section VII) appeared to a greater extent in the siblings than in any of the other relatives—2.1% of the brothers and sisters of 7% of the patients; but no startling relationship was indicated between feeblemindedness and the other neuropsychiatric conditions enumerated (Tables II and IV and Figs. 2, 3 and 4).

8. *Alcoholism.*—Alcoholism (Section VIII) appeared mostly in the fathers of both patients (22.2%) and controls (5.2%) but, like migraine in mothers, there was no constancy of alcoholism with respect to seizures in the other members of the family, *i. e.*, siblings.

Alcoholism at the time of conception was admitted in only 12 cases or 1.2%, a figure which is doubtless far from the truth.

9. *Psychosis.*—Psychoses, other than those of epilepsy, mental deficiency, and alcoholism, appeared in small proportions throughout. The incidence of psychosis for any and all relatives was only 7.8% of the patients. This was more than twice as much as the similar incidence in any relation of the control group (3.7%). If the psychoses of epilepsy, feeblemindedness and alcoholism were included the incidence would be nearer the usual expectancy for psychoses in the community.*[18]

10. *Miscellaneous Neuropsychiatric.*—The Miscellaneous Neuropsychiatric conditions enumerated in detail in Tables V, VI and VII—Section X, are included, along with the other neuropsychiatric data studied, for completeness and to indicate their relative values. They may be summarized as follows:

A. Organic nervous diseases (42.1%).
B. Nervousness, nervous breakdown or hysteria (24.8%).
C. Miscellaneous (functional, emotional and social) (33.1%).

Better memories and more uniform opinions on just what does constitute a "very nervous," "immoral," or "hysterical" person, as well, of course, on the identity of many infantile fevers and diseases of early childhood, would undoubtedly affect these lists considerably.

11. *Total Neuropsychiatric.*—However, even if we deduct this miscellaneous group, the total neuropsychiatric group does stand

out as being consistently between two and five times greater in the family histories of the epileptics than in those of the controls regardless of whether the incidence is calculated per individual, *i. e.*, according to the number of patients or families represented, or per total number of relatives.

Comment.

Conclusions depend largely on one's interpretation of what constitutes heredity; hence, before concluding, it is necessary to recall that there are two viewpoints on the subject. The older point of view is that the condition, epilepsy, is passed on in its complete form from parent to child. Thus, if there is no history in an antecedent for one or two generations back, there cannot be said to have been any heredity.

The newer point of view is that not the epilepsy *per se* but a tendency or constitutional weakness is passed on from the ancestor to the offspring, *via genes* in the germ plasm (predisposing factor).

Whether or not a person develops seizures depends on the presence or absence of certain controlling factors (exciting factor).

This idea is expressed by Jennings (15) as follows: "There is a common impression that a disease or defect that is hereditary is inevitable, inescapable; that it is a factor against which the individual cannot struggle . . . . even though a hereditary or genetic basis exists for a defect or a disease, that defect or disease need not actually come into existence. . . . . What the individual inherits is a constitution that under certain conditions will produce the disease; under others it may not."

Theoretically, then, to find out one's susceptibilities one would have to subject all of the relatives of patients to some stimulus like a convulsant drug, to find out whether or not they would develop epilepsy.

Practically, however, "the study of identical twins has helped to elucidate many problems bearing on the incidence of heredity and environment," write Wilson and Wolssohn (38) in their excellent paper, "Organic Nervous Disease in Identical Twins." "It is not easy," they continue, "to account for the same mental illness affecting identical twins at about the same time and evolving in the same way, unless one accepts the doctrine of the inherent potentiality of certain types of mental disorder."

As yet, however, the cases of epilepsy in identical twins are far too few in number for any worthwhile or sweeping conclusions.*[3]

Conclusions also depend upon which of the figures given one may choose to use. Thus, practically all of the neuropsychiatric disorders enumerated appear in the family histories of the epileptic group from between two and five times as frequently as in the family histories of a similar number of controls.

On the other hand, 18.1% of the patients give a positive history of seizures in parents, siblings or children; but out of the total number of 6572 parents, siblings and children, only 240 individuals, or 3.6% had these seizures, and considerably fewer numbers were actually epileptics. These are presented graphically in Fig. 5, *q. v.*

Stated differently, 81.9% of the 1000 patients gave no history of seizures in their immediate family; and of their 6572 parents, brothers and sisters, and children, 96.4% gave no history of seizures.

Conclusions.

I. The results of this study do not justify the conclusion that the symptom-complex known as epilepsy, either *per se* or as migraine, or as any other neuropsychiatric disorder, is an inherited condition.

II. However, the higher incidence of neuropsychiatric disorders in the families of epileptics may well be explained on the basis of an existing potential or latent germ-plasm defect. It is likely that this defect or vulnerability furnishes more than usually fertile ground for the production of epilepsy by such known contributing factors as trauma, infection, birth injury, alcoholism, etc. In other words, it may be that this potential or latent germ-plasm defect, whatever it may be, requires a less severe blow than usual from the above named contributory or exciting factors, in order to activate it into the clinical condition known as epilepsy.

III. It is difficult to escape the conclusion that this germ-plasm defect or vulnerability appears in too large a proportion in the family histories of the patients, when compared with those of the controls, to be entirely accidental.

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DISCUSSION.

DR. S. BERNARD WORTIS (New York City).—Let me thank Dr. Stein for his excellent study—it represents a challenge to our therapeutics in epilepsy.

DR. HORATIO M. POLLOCK (Albany, N. Y.).—Mr. Chairman, I think this is an exceedingly interesting study and I was especially pleased with the conclusions reached by the writer. I think, however, that one or two re-

flections ought to be made concerning the study of the material. Evidently the full life history of the cases studied was not available to Dr. Stein. In several cases probably the life cycle was not completed and some of the disorders to which he referred would undoubtedly appear later in life. I refer particularly to the psychoses. The rate of the psychoses in Dr. Stein's control group was very low. I think better data are available in regard to the occurrence of psychoses in the general population. I refer particularly to a study of the expectation of mental disease which was made in the New York State Department of Mental Hygiene a few years ago in which after a study of a large group of cases covering a considerable period we found that the general expectation of mental disease including all groups, was approximately 4.5%. Among men the expectation was 4.7% and among women, 4.4%. These rates are much higher than those shown by Dr. Stein for his control group. I believe they present a more accurate picture of what may be expected in the population in general.*[10]

Dr. D. S. Renner (Skillman, N. J.).—Mr. Chairman, I would like to ask Dr. Stein how he identifies the fathers. That has been the hardest job I have had in trying to gather statistics on epileptics. It has been absolutely impossible for me to identify them. Probably it is in New Jersey, but I am asking for information from Dr. Stein.

Another thing that I am inclined to think plays a very important part in the so-called heredity of defective germ plasm is not the chronic conditions that afflict the parents but the severe toxic conditions from which either the mother or father might suffer at the time of conception of the child, or the many toxic conditions that the mother might suffer during the time of gestation. It is a little easier for us to identify the mother than the father; consequently, I think that fact accounts for the difference in Dr. Stein's statistics on that point.

Dr. Robert F. Sheehan (New York City).—I have been very much interested in these observations. We have been much interested in the relation of trauma to convulsions and are working at present to prepare results of our statistics. Along this line we have endeavored to ascertain the effects of labor. For a long time it has been my own belief that what is called normal labor results in considerable cerebral trauma to the child.

We have been confronted with the same difficulty that Dr. Renner has just mentioned in identifying the father. In hospitals such as the New York Foundling and Misericordia, of New York, which have large obstetrical services and where we have many infants with convulsive attacks, we have found the material that we are utilizing.

I was interested in the remarks of Dr. Gordon in which he mentioned carbon monoxide poisoning as the cause of an anoxemia, and stated that because such cases do not have convulsions from carbon monoxide poisoning, this eliminates carbon monoxide as a factor. I do not agree with that. Carbon monoxide poison is par excellence the cause of an anoxemia but in those cases where there is severe carbon monoxide poisoning, they die; they

do not have time usually to have a convulsion. But let us think of the anoxemia that may be due to deprivation of oxygen and probably excessive carbon monoxide such as occurs in labor. I expect that the effects on the cortex will be seen long afterwards. I also consider that probably the convulsive seizures that we see following trauma may be due to the same motivation.

Also I was very much interested in the variance of opinion as to the importance of dehydration. My own inclination judging from our work is that convulsive seizures may be attributed to brain trauma with a consequent disturbance of cerebral circulation, not necessarily an anoxemia, or an excess of fluid, but other factors doing damage.

Another point that I think is important is that in hundreds of cases which we have had as the result of trauma (fracture of the skull or cerebral concussion), the similarity of the clinical pictures will be found to be striking. The patients give a story which sounds almost as if it were rehearsed. We have checked this with the barometric findings, temperature and humidity, and on days when the barometric pressure is high, the patients all feel worse. They have more headache, are more dizzy, and they are subject to attacks which may be merely of vertigo but in some cases they do fall and apparently have a convulsion. I think these factors are of importance and I trust that within the next year we may be able to present to you our results of this work.

Dr. D. M. Levy (New York City).—There are a number of difficulties in the accumulation of the data with which, I am sure, Dr. Stein is quite familiar. Nevertheless, I think they ought to be brought out quite clearly. In the first place, he is dealing with 612 epileptics, if I remember the Monson figures rightly, mostly feebleminded who come to the institution 12 or more years after the initial seizure, most of them of a low economic level. He is comparing them with a control group of 190-odd in which I assume a similar social and economic grade to make the comparison fair. From these patients, who represent poor material for getting information, and, as Dr. Renner pointed out, in whom even the question of paternity is very doubtful, the whole picture given seems to yield the definite conclusion, namely, that if a person at Monson has epilepsy, the chances are that you won't find another epileptic in his family oftener than 1 in 25 times. I think that is the significant fact presented and that it is sufficient to show that epilepsy is not inherited like a mendelian character, or related to migraine as a recessive to a dominant trait. In regard to migraine, since I have made a statistical investigation of its frequency, I can the more readily understand the difficulty in getting accurate information.

The theory which discounts the inheritance of epilepsy as such, but which regards the epileptic generally as an individual who comes from a stock likely to explosive symptoms, whether in the form of chronic epilepsy, infantile convulsions, migraine, fainting spells or even severe temper tantrums, seems to me convincing, especially in the light of these studies that show a relationship between infantile convulsions, epilepsy, marked temper

and the other symptoms mentioned. Hence, I would like to utilize the point about migraine in order to show that the possibility of such a relationship is by no means ruled out by this study. If you try to get a census of migraine by making a study of sample groups in cities and country towns, you will find soon that you include in your definition of migraine chronic periodic headaches starting in the teens, accompanied by the typical visual, gastro-intestinal, and equilibratory symptoms. If you compare the migraine in such a census with office migraine as diagnosed by the neurologist, you will find a very similar alignment of symptoms. If you question carefully, you will find that the majority of women give a history of migraine. I found as high as 50 to 60% in three different communities, and I am sure the percentage was inaccurate and low. Since most of these headaches were of a mild degree, the interest is centered in the severity of the headache rather than in its presence.

In classifying migraine headaches that come once a month or oftener with less frequent forms, I try to study in relation to the two groups of parents so afflicted, the incidence in their children of infantile convulsions, fainting and certain severe forms of temper tantrums, namely, temper tantrums with head-banging or breath-holding. There was a significantly larger number of these so-called explosive phenomena in the children of parents in the group of higher frequency of migraine. The same relationship was found among parents who fainted, as compared with those who didn't. The difference was significant enough to conclude that the chances of a child having infantile convulsions are greater than normal if the parents, mother or father, or both, have frequent migraine or fainting spells.

Dr. Douglas A. Thom (Boston, Mass.).—I was very much interested in Dr. Stein's presentation. I think what he terms hereditary influence depends on the instruments of precision that we use. I remember some years ago, I think in 1915 or 1916, I selected 130 epileptics that had married, and studied the offspring. As I recall, there were 532 children in that group, and the incidence of convulsive disorders was relatively small. Seventy-five per cent of these children were beyond the age where 80% of the epilepsies begin or in that epileptic range, that is, over 20 years of age.

There are many factors relative to heredity that are difficult to measure, such as alcoholism. A woman who perhaps drinks moderately may be called an alcoholic, while a man may drink excessively and still be able to keep on his job and fit into the social scheme of things and get by as a moderate drinker.

I would stress the point very strongly that Dr. Pollock made, that is that we have sufficiently well worked out statistics on the relative frequency of feeblemindedness among the general population or the psychoses and in other factors that are probably very much more valuable as controls for Dr. Stein's work than the relatively small figures that he has presented, even combining with those of Dr. Lennox.*[10]

The important thing, I think, is that all those who have been working in the field of heredity, have plotted general curves of the whole situation

that are radically different from those which were presented to us by the group under Dr. Davenport many years ago. We are unable to interpret many of these neuropathic, neuropsychiatric difficulties in terms of heredity.

Dr. Hugh E. Kiene (Philadelphia, Pa.).—I would like to ask a short question. In the study of the families of epileptics. Has Dr. Stein gone into the incidence of rickets, particularly on the maternal side? It seems to me that such a study is indicated since there is considerable discussion as to whether a birth trauma is very often the precipitating factor.

Dr. Calvert Stein (in closing).—I am grateful to the discussers for taking up in their remarks what, because of lack of time, I was unable to present in the body of the paper; namely, a review of the literature. In the section on histories there is reported a discussion by Dr. Burr in which he refers to the difficulties in getting accurate histories, and in fact in placing too much emphasis on any kind of history. The story is this: You have to depend upon what people tell you. You have to depend upon what people tell you at different times; and every historian knows that the same story is never told twice in the same way, and that people are apt to color or favor one side of their family history more than the other. They may have a prejudice, for instance, against the husband, who may be among the missing. In speaking of absent husbands, the question was asked, how we managed to trace the fathers; and the answer is, we don't (*i. e.*, we don't have to). It must be remembered that these are completed case histories; and I do wish to correct the impression that we received at Monson only a group of ignorant, feebleminded castaways. That is not true. It is perfectly true, however, that about one-half of the admissions to Monson do fall into the feebleminded class, but we don't know that this feeblemindedness began after the epilepsy; for you will remember that epilepsy is a disease essentially characterized by deterioration, and the mere fact that we are obliged to report as feebleminded about one-half of the admissions for each year does not necessarily mean that they all start out that way.

One more point in regard to the histories—Dr. Burr also stated that to be of any value a history should take in three or more generations with a full story on each. Dr. Thom, in the study to which he referred about 17 years ago, did succeed in doing that. He found about 21 cases with epilepsy in the patients and with known epilepsy in one or more of the grandparents. Out of that group of 21 cases 7 showed epilepsy in the middle generation, that is, in the parents, or about one-third of the cases with three generations of epilepsy. Those figures are startling and they are significant, but remember they are only for 21 cases.

I told you at the beginning that we started with only 190 controls. If you add the other 272 controls of Dr. Lennox, that makes a total of 462 controls and I think that this is a figure which one might take into some consideration. Dr. Minkowska, a German physician, published about a year ago in French an account of 1000 relatives taken from two family trees which began their history in Switzerland about the year 1775. One of them, the

paternal great-great grandfather was a known epileptic and the other, the maternal great-great grandfather, was a known psychotic. Just which psychosis was not stated except that it was inferred to be schizophrenia. In the 1000 relatives she was able to trace—and her methods, by the way, were those of word of mouth in a small community in Switzerland where apparently everybody knows everybody else's business—she ascertained pretty well just what had been going on through a good many generations. She reported only eight epileptics in the entire group. As to the effects of labor on seizures in the children, I cannot tell you what percentage occurred in our histories. The same is true for alcoholism at the time of conception (see Section VIII). I recollect it occurred in a relatively small percentage, and here again you have to take only what people tell you, if you want to believe that. With anoxemia in labor, and its effects on the cortex, this paper was not concerned. No study was made on rickets in mothers.

The statistics on migraine, you remember, I told you were almost the same for the mothers of the controls as for the mothers of the patients. I also said they were open for conjecture. Their relationship to temper tantrums and breath-holding spells was not considered in this study.

As to the incidence of psychoses our figures were quite low, only one-half of 1% for the immediate family of the controls and 0.6% for all members of the immediate family of the patients, but about six times as frequently for other relatives of the controls. Remember, that this was a study of only 190 control cases (Dr. Lennox's 272 cases were not available for this part of the study). Dr. Hodskins, about two years ago, gave an estimate of an incidence of about 1 in 390 for epilepsy in western Massachusetts. The incidence of psychoses is undoubtedly higher and this number of 190 cases was, of course, much two small to be used as a criterion for these particular data (see new figures for 772 control histories—Section IX and Tables III and IV.)

Replying to the last question, relating to birth trauma as a precipitating factor, no study of that was made in this survey.*[3]

EXPERIMENTAL CONVULSIONS FOLLOWING LESIONS OF THE TUBER CINEREUM.*

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Different anatomical nuclear masses are from time to time designated as "centers" capable of causing generalized epileptic seizures. Some have based their conclusions on a study of the brains of persons known to have been afflicted with convulsions during life; others have induced generalized convulsions by various experimental methods and arrived at totally different concepts. Recently some workers have come to view aberrations in function of the nuclei in the region of the tuber cinereum as the causative pathology in epilepsy. A brief analysis of this viewpoint follows.

Anatomy and Known Physiology of the Region.

In embryological development several structures arise from the hypothalamic floor—in order, these include: the infundibulum, tuber cinereum, and mammillary bodies. The diencephalic nuclei which are known to control autonomic functions are located in the wall of the third ventricle and the hypothalamus. This region is comparable with the paleothalamus of lower vertebrates and acts as the highest regulatory center for visceral functions. (Tilney and Riley, Kraus, Kuntz.) [18]

Malone (1910) [23] and Greving [9] (1923) have given us most information concerning the anatomy of this region. The tuber cinereum is made up of three large cellular groups which include: (1) the substantia grisea lateralis, (2) the nucleus supraopticus, and (3) the nucleus paraventricularis (Malone).[23] According to

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Kuntz [18] "the constituent neurones of these nuclei resemble very closely the visceral efferent neurones in the spinal cord and medulla oblongata; consequently, they may be classified as autonomic on the basis of their morphological characters." Other neighborhood nuclei, the nucleus mammillo-infundibularis (Malone) have similar cells and from experimental evidence may be regarded as having autonomic function. Work by Ott [26] (1891), Leshke [21] (1913), Karplus and Kriedl [16] (1909, 1918), Eisenschmidt and Schnitzler (1914), Warner [35] (1931), Kraus [17] (1931), Bailey and Bremer [1] (1921), Richter [29] (1930), Crowe, Cushing and Howman [4] (1910), Camous and Roussy [2] (1920), Morgan and Gregory [24] (1930) would seem to indicate that the regulating centers for water and salt elimination (diabetes insipidus), fat metabolism, vasomotor function, and possibly temperature regulating mechanisms are located here. Greving [9] regards the autonomic diencephalic centers and the pituitary gland as a functional unit.

Experiments in Brief.

L. O. Morgan [25] and his coworkers (1930) have induced generalized convulsive seizures in dogs by making lesions in the region of the tuber cinereum. For this purpose they use 0.1 to 0.2 c. c. of a 0.3 per cent solution of mercuric chloride injected by way of the parietal lobe or through the orbit; generalized convulsive seizures resulted within two to six hours after injection. Morgan implies that such a lesion in the tuber cinereum is irritative and causes a discharge of impulses from the nuclei *specifically* resulting in fits. He also believes that "destruction of a large area in the tuber cinereum would no doubt give different symptoms from those produced by introducing a reagent which might set up an irritation."

In the Bellevue Hospital Laboratory of Experimental Neurology we have been able to confirm the production of such convulsive seizures and further investigate this problem.

Material and Methods.—The cat was used as the experimental animal. Under light ether anesthesia—after washing the eye with a 1 per cent silver nitrate solution—a needle was inserted through the orbit and back via the optic foramen to the base of the tuber cinereum region. In some animals a temporal trephine approach was used—the brain raised and the tuber cinereum region ap-

proached by way of the base. In both cases destructive lesions (traumatic or excision) were produced in this region.

Several control animals were injected with 0.1 c. c. of a 0.3 per cent solution of mercuric chloride in this region and some had convulsions as Morgan describes. All animals that died were autopsied, the brains were fixed in bromoformal and sectioned for microscopic study.

Twenty-four cats were so operated upon and in eight were localized destructive lesions placed in the tuber cinereum region as proved by examination of the brain.

Convulsions were induced by the intravenal injection of a standardized solution of camphor monobromide. This technique has been previously reported.[36]

We have accordingly made destructive (puncture) lesions in the same area Morgan mentions and at subsequent time periods (after anesthesia effects have worn off) have been able to induce generalized seizures in animals, following injection of a standardized convulsant drug (monobromated camphor) by vein, electrical cortical stimulation (in one instance) or ligation of the head arteries (in one instance). Also the injection of mercuric chloride in amounts similar to those used by Morgan into the region about the *motor cortex*—without causing involvement of the tuber cinereum by an "irritative" hemorrhagic necrotic lesion—results in seizures in many instances. These findings would seem to negate the specificity of lesions of the tuber cinereum as the only cause of generalized convulsions. In addition the following evidence is offered.

Discussion and Conclusions.

Review of the literature would seem to impose the fact that generalized convulsions can be "set off" by various disturbances in different parts of the central nervous system. Histological examination of epileptic brains has not cast suspicion on any one specifically localized lesion. Jakob (1914), Bratz (1920), Gerstmann, Volland, Kogerer (1923) and Spielmeyer (1926) have all more or less contributed to the belief that the pathological findings have no specific interest because they are also seen in other conditions. However, Spielmeyer found small areas of destruction in 80 per cent of 126 epileptics—in Ammon's horn and the cerebellum and

believes they may be the result of angiospasm. L. O. Morgan [31] from a study of 27 human epileptic brains would seem to predicate disease of the tuber cinereum nuclear regions acting as the irritative focus causing epilepsy.

Penfield (1930), Globus and Strauss [32] (1931), Horrax (1930-Nelson's L. L. Med.), Fulton and Bailey [8] do not stress the unusual frequency or infrequency of convulsions associated with tumor growths in this region. Penfield's case of autonomic diencephalic epilepsy had generalized convulsions. Globus and Strauss [32] report three cases with tumor in this region, associated with abnormally high temperatures but make no mention of convulsive seizures. We are all familiar with convulsions associated with third ventricle or suprasellar neo-plasms, and know that fits do not always occur in these cases. Maranou and Pintos (1916) [8] reported the case of a bullet lodging in the mid-line tuber cinereum region—following which the patient, a young boy, had diabetes insipidus, became fat and exhibited arrested sexual growth—but had no convulsive seizures.

Sudden cerebral anemia (*i. e.*, cerebral anoxemia) has long been known to be a cause of convulsions. Kellie (1824), Piorry (1826), Ashley Cooper (1824), Kussmaul and Tener (1857), Leonard Hill (1895) and Gildea and Cobb (1930), all were able to induce generalized fits by various procedures resulting in cerebral anemia. Robert Lobel (1926) in studying metabolism of brain tissue was able to demonstrate that the oxygen consumption of brain tissue is high as compared with other organs. Animals can be given convulsions by limiting the inhaled oxygen. Lennox and Cobb in their excellent monograph believe that anoxemia, which is the result of anemia, is probably a basic factor. This would seem to be further substantiated by their study of epileptics—wherein those subjected to oxygen-poor air (12 to 14 per cent oxygen) had many convulsions, whereas such seizures could be diminished by causing the same patients to respire in an oxygen-rich atmosphere. However a diminished oxygen supply in normal persons is not sufficient, of itself, to cause a convulsion as shown by Schneider and Truesdale (1921) in their series of respiratory tests on aviation recruits, most of whom lost consciousness when the oxygen content of the air reached 7 to 8 per cent.

Focal brain stimulation by different methods has been known to produce generalized fits. Landois (1887) spread keratin and other urinary products over the surface of the brain. Bichel (1898) used bile pigments in similar fashion and also induced generalized convulsions in animals. Leibig's extract (Karangi and Tauszk, 1890), strychnine painted on the brain cortex (Baglioni and Amantea, 1914, and also Amantea, 1912), CO_2 to freeze cortical areas (Speransky, 1926), mercuric chloride (L. O. Morgan, 1930) and electrical stimulation (Fritsch and Hitzig, 1870 and Ferrier and Horsley, 1873, Sparks, 1927, E. Spiegel, 1931, Foerster, 1927) have all been used successfully to produce generalized convulsive seizure in animals.

Trauma with resultant brain scarring has been shown to be the cause of generalized convulsions often having focal origin. Foerster, Penfield, Del Rio Hortega, Bagley, Stevenson, Wortis and others have demonstrated the associated brain pathology possibly originating convulsions in this group.

Various substances (absinthe, camphor, acid fuchsin, cocaine and picrotoxin) capable of causing convulsions by their intravenous or oral use have been studied by Victor Horsley (1885), Hughlings Jackson (1887), Ziehen (1886), A. V. Hill (1900), Muskens, Pike,[27] Syz, Wortis [36] and others. Alkalosis, asphyxia, and cerebral edema are known causes of convulsions and have been stressed by many workers.

" Vascular spasm " of the cerebral vessels has often been postulated as the " common mechanism " whereby all the accepted known causes of convulsions act. This hypothesis depends in large part on the fact that various observers (notably Foster Kennedy and Hartwell, Foerster and others) have seen in the exposed brain a preparoxysmal cortical blanching associated with diminution of brain volume—the convulsion then occurring with brain swelling and associated venous engorgement. In addition it should be emphasized that in the experimental laboratory many (McDonald and Cobb, Pike, Coombs and others) have also noticed some degree of cortical vasoconstriction in the period just preceding the motor evidences (tonic or clonic) of a generalized fit. The well known skin and mucous membrane blanching occurring at the same time is surely another evidence of vasoconstriction. These reactions in all probability represent vasopressor stimuli passing out of

the central nervous system by way of the sympathetic nerve fibers which go to control the caliber of the vessels (to brain and skin) in these areas.

Work by Bazett and Penfield (1922), Woodworth and Sherrington (1904), Cannon, Britton and Lewis (1924-1927), and Bard (1929) would seem to indicate a diencephalic representation of the sympathetic nervous system. Karplus and Kriedl (1909-1927) found in cats that stimulation of an hypothalamic point lateral to the infundibulum produced maximum pupillary dilatation, profuse sweating of all four limbs, and a rise in arterial pressure. They further showed, that in addition, these effects are carried out by way of the sympathetic nervous system.

The work of Beattie, Brow and Long (1929-1930) would seem to indicate that the hypothalamic region has nuclear centers which control fat metabolism and water and salt metabolism (diabetes insipidus); and Bard (1928) has shown that spontaneous "sham" rage can no longer occur in animals which have been deprived of this region surgically.

Stimulation of sympathetic nerves has long been known to produce constriction of the related small arterio-capillary bed. Hooker (1921) first demonstrated this in mammals (the cat) by stimulating the cervical sympathetic nerves and noting the resultant capillary constriction in the depilated ear on the same side. Harris and Marvin (1927) confirmed Hooker's findings. Weber (1908) in experimenting with cats found a decrease in brain volume following cervical sympathetic stimulation. Brachet (1830), Fiegerstedt (1923), Florey (1925), Talbot, Cobb, Lennox and Wolff (1927-1929) have shown (as Hill formerly believed) that strictly speaking "there is no evidence of a causation of cerebral anemia by spasm of the cerebral arteries." Further they have demonstrated that even though cervical sympathetic stimulation can cause reduction in caliber of pial arteries that "real obliterating angiospasm has only been experimentally observed when vessels are strongly and locally stimulated under non-physiological conditions." Cobb has shown that according to Poisenilles Law (1842) the minute volume flow through a given length of capillary tube varies directly with the 4th power of the diameter of the tube. Therefore with a given 8 per cent (Forbes and Wolff 1928) decrease in pial vessel diameter on cervical sympathetic stimulation there would be

approximately a 40 per cent decrease in blood flow. One must remember moreover that these represent non-physiological conditions. Many conditions which result in cyanosis (*i. e.*, diminished oxygen content of blood), pneumonia, advanced phthisis, pneumothorax, lung embolus, asthma, congenital heart disease, lung neoplasm, drug poisoning causing methæmaglobin increase (viz., veronal, trianol, sulphanol, phenacitin) are seldom attended by convulsions. However, complicating toxic or acidotic states may well be active. In addition normal persons breathing air of low oxygen content lose consciousness but do not have convulsions (Schneider and Truesdale, 1921). However small degrees of cerebral vasospasm can occur physiologically and may cause sufficient metabolic (anoxemia) changes to "set off" convulsions, only in "susceptible" persons.

Meagher and Ingraham (1927) showed that faradization of the cervical sympathetic trunk in the rabbit and cat—on one side—in the presence of ligation and division of the common carotid artery of the opposite side, is unattended by convulsions. Pike and Wortis (1931) have demonstrated that experimental camphor convulsions can be induced in animals (cats) following bilateral cervical sympathectomy by the use of standard solutions of oil of absinth or camphor monobromide. Furthermore following unilateral cervical sympathectomy such experimentally induced convulsions are bilateral, and start simultaneously on both sides of the body. Clinical results of cervical sympathectomy on epileptic patients have been disappointing (Alexander, 1889, Wagner, 1925, Hirsch, Weiss, Izgur and Lanerman, 1927). It would therefore appear that although there are, in an epileptic convulsion, many evidences of "discharge" occurring over sympathetic nerve pathways producing resultant vasospasm, such vasospasm is not always of itself the cause of the epileptic fit, but may well be an early expression of the fit having already started.

Endocrine abnormalities or diseases of the gastro-intestinal tract are apparently not more common in epileptic than in other patients. Although a few cases are on record of epileptiform convulsions due to hypoglycemia caused by pancreatic (*i. e.*, islet) adenomata.

Metabolism studies in epilepsy are as yet fragmentary but would seem to indicate that carbohydrate metabolism is not affected. Lennox and Cobb,[20] in reviewing the literature, say that "there is

no conclusive evidence of disordered fat metabolism in epilepsy." Protein metabolism requires further investigation. Although allergic phenomena have been reported by many (Foster Kennedy, Zabriski and others) these would appear to be present only in the occasional patient. Further studies in this regard would be most valuable.

Many substances capable of causing dilatation of the cerebral vessels do not inhibit convulsive seizures in patients. In experimental animals, amyl nitrite inhalation, cervical sympathectomy, or the intravenous injection of ergotoxin, do not prevent the occurrence of experimentally induced convulsions with standard convulsants (absinth or camphor). On the other hand, some drugs known to produce arterial contraction do not induce convulsive seizures—among these may be listed pituitrin or the intravenous injections of hypertonic solutions. Moreover the well known convulsant action of large doses of insulin causing hypoglycemia—is not explained by " vasospasm."

Stanley Cobb [3] has recently tabulated no less than 56 clinical causes of convulsions and utilized 13 physiological mechanisms to explain the genesis of such seizures. He believes impaired conduction of cerebral tissue and cerebral anoxemia constitute the major functional defects. Possibly drug fits may be found to fit into a related mechanism.

With all the aforementioned evidence it seems highly improbable that there is one specific " convulsogenic center " in the brain, responsible for all convulsive phenomena.

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A BRIEF DESCRIPTION OF PSYCHIATRIC CONDITIONS IN MASSACHUSETTS.

For the Orientation of Those Attending the 1933 Meeting of the American Psychiatric Association.

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"Name the New England states." This is a test commonly applied in psychiatric examinations in the region where the next meeting of the American Psychiatric Association will be held. Failure to name these states correctly is only less serious than the inability to give one's name and address. New England is much more than a geographical concept, much more than a political subdivision. To paraphrase the old statement about Boston, "New England is a state of mind."

From the landing of the Pilgrims to the present time, there has been a unity of thought and feeling in this section of the country; it has been closely knit as a result of its historical, political, and economic life, as well as educationally and medically. Misusing psychiatric nomenclature, it may be said that the New England states are one genetically, and quite unified dynamically.

It is this whole region, then, that bids welcome to The American Psychiatric Association in its forthcoming meeting at Boston, which happens to be the metropolis of New England. The members of the Association living in New England wish to be looked upon as hosts to the visiting members. The staffs of the psychiatric institutions throughout New England are desirous of having the members visit them so that they may show them the courtesies of the several institutions.

Those visitors who will extend their stay and tour New England will find psychiatric institutions scattered along the course of their journey as pivotal points to visit. One may suggest a great number of trips through Massachusetts and New England of interest to lovers of history, nature and sport as well as the more serious minded psychiatrists. For instance, one very interesting route would be to the Vermont State Hospital at Waterbury, Vermont. Leaving Boston, one would pass Wellesley College on the way to Worcester, where is located Worcester State Hospital, one of the most active medical and psychiatric institutions in the United States. From Worcester,

a short run brings one through Amherst, the site of Amherst College, to Northampton, the home of Smith College. In Northampton are located Northampton State Hospital, which serves the western part of Massachusetts and which cares for a large part of the rural community of the state, and the United States Veterans Hospital. Only a short distance from Northampton are the Monson State Hospital, for the care of epileptics, and the Belchertown State School for the Feebleminded, both of which may be reached by alternate routes from Worcester to Northampton.

From Northampton, the route is over the famous Mohawk Trail, one of the outstanding scenic routes of the country, into the delightful Berkshire country; passing through Williamstown, the home of Williams College, and thence into the state of Vermont. This state is worth visiting from the standpoint of its historical land-marks, its extraordinary rural scenery, redundant with lakes, rivers, and dominated by the Green Mountains. Reaching Waterbury, one may well visit the Vermont State Hospital which, with the Brattleboro Retreat at Brattleboro, cares for the psychiatric problems of the state.

From Waterbury, one can swing across into the White Mountains of New Hampshire. Any New Englander will maintain that there is no more beautiful scenery in the world than that offered by the White Mountains.

Leaving the White Mountains, one drives through the lake country of New Hampshire to Concord, the capital of the state. In this city is found the Concord State Hospital. At Concord, one is only eighty miles from Boston to which city one can drive over the route made noteworthy by Paul Revere in his famous ride, passing in this last lap of the journey, the United States Veterans Hospital at Bedford and the new Metropolitan State Hospital at Waltham. Just before reaching Boston, one arrives at the McLean Hospital which has the distinction of being the oldest psychiatric institution in New England. In Cambridge, before crossing the bridge to Boston, one sees Radcliffe College, Harvard University and the Massachusetts Institute of Technology.

Another tour may be suggested through the state of Maine. A few miles from Boston one comes to the Danvers State Hospital which should be particularly well-known to the members of the Association as the training center and work place of several past presidents of the Association; namely, Barrett, Southard, Mitchell, Kline, and Bond.

Continuing from Danvers, one soon leaves Massachusetts for a strip of New Hampshire only eighteen miles in width to reach the state of Maine. This state, well-known as the summer playground of the nation, contains almost as much water in the form of lakes and rivers as land; and it has almost four hundred miles of rock-bound coast-line indented with bays and harbors with numerous islands off shore. It is the home of many summer camps for boys and girls. One passes along lakes and rivers and forests to Augusta, the site of the Augusta State Hospital; then north to Bangor and the Penobscot River on which is located the Bangor State Hospital. From Bangor, one may suggest a visit to Bar Harbor and Mount Desert Island, or one may continue one's tour up into northern Maine, through beautiful rolling

hills, heavily wooded, along some of the finest waterways and lakes to be found anywhere. To the followers of Isaak Walton, this is the country of choice; salmon, trout, and bass fishing is at its best in this region.

It one wishes to tour a more sophisticated region, one may go through Rhode Island and Connecticut. From Boston one would go to Providence, the home city of Brown University and Butler Hospital. Nearby are such resorts as Newport and Narragansett Pier. From Providence, it is but a few miles to Howard, the location of the State Hospital of Rhode Island. Thence one travels through the tobacco country of the Connecticut Valley to the Hartford Retreat near the capital of Connecticut, through Middletown, the home of Middletown State Hospital, to New Haven, where connected with Yale are the new Psychopathic Hospital and the Institute of Human Relations. On reaching New Haven, one is on the outskirts of New England, where the influence of New York can already be felt and possibly the tourist will be lured to New York City.

It is almost unnecessary to remark that through all New England are many fine golf courses for the lover of this sport.

It is not possible to enumerate many other interesting tours or to mention all the institutions for we must turn to the more serious consideration of the psychiatric set-up of Massachusetts.

The history of the care of the mentally afflicted in Massachusetts closely parallels the history of psychiatry in the United States. While Massachusetts was not the first locality to build institutions for the care of the mentally afflicted, this problem was taken up rather early. The first institute of this sort to be established in New England was the McLean Hospital which opened its doors for the admission of patients in 1818, or 115 years ago. This was only 26 years after the revolutionary work of Pinel, and only six years after the publication of Rush on "Medical Inquiries and Observations upon the Diseases of the Mind." The Connecticut Retreat was opened in 1824, and in 1833, the Commonwealth of Massachusetts built its first hospital for mental diseases at Worcester.

Funds for the McLean Hospital were obtained by private subscription but assisted by a grant from the state. From the beginning, McLean has been an institution supported partially by donations and partially by the pay of the patients, but run entirely as a community enterprise under a board of trustees appointed in part by the corporation and in part by the governor. In an article entitled "The History of Insanity During the Past Century with Special Reference to the McLean Hospital," Dr. C. MacFie Campbell calls attention to what has been the guiding principle, not only of McLean, but of the mental hospitals of Massachusetts; namely, the

humane attitude. Dr. Campbell quotes from the report of Dr. Wyman, the first superintendent of McLean:

> It is believed that the people have much to learn regarding lunatics—that insanity is curable—that a few weeks or months are not sufficient for a reasonable trial, that absence from home is always indispensable—that whips and chains are forever banished from every well-regulated asylum for the insane.

The importance of occupation and diversion was also recognized early and as Dr. Campbell records, the 1829 report of the McLean Hospital shows an expenditure for medicines of $32.79 and for diversions of $1,089.68.

The present site of McLean Hospital at Waverly was first occupied in 1895. McLean Hospital established the first training school for nurses in a hospital for the insane in 1892. In 1900, Dr. Otto Folin established a chemical laboratory and in 1904, a psychological laboratory was opened by Dr. Franz. Throughout this period of 115 years, McLean Hospital has been an outstanding example of an institution giving humane care to mental patients and at the same time it has kept abreast of modern investigations, as well as pioneered.

There are a number of private hospitals for the care of nervous and mental diseases in the Commonwealth of Massachusetts, all of which are required to live up to a standard set by the Department of Mental Diseases of the Commonwealth of Massachusetts. However the care of the vast majority of the cases with mental disease has devolved upon the Commonwealth itself. Probably no where else in medicine has the state taken such a large share of responsibility as in the care of the mentally afflicted. Although I have no adequate statistics at hand as to the exact number of patients in private hospitals, it can be safely stated that the number is less than 500, whereas for November 30, 1931, there were 23,385 patients under care in state institutions. To care for this large group of patients there have been developed in Massachusetts 16 special institutions, of which 12 are for the care of various mental diseases, one a special institution for the care of epileptics, and three institutions for the care of mental defectives. As already mentioned, the first state hospital was opened in Worcester in 1833, the second

institution was opened at Boston in 1839, but was a city institution and was not taken over by the state as the Boston State Hospital until 1908. These state hospitals are under the supervision of Boards of Trustees appointed by the governor.

As the number of institutions multiplied and the number of patients to be cared for increased, it became apparent that some central control or supervision was desirable. In 1863, a state board of charity was established and for the first time the insane in Massachusetts came under central supervision. This board was later superseded by the State Board of Health, Lunacy, and Charity. In 1898, the State Board of Insanity was formed, to be reorganized in 1914, and finally in 1916, the Massachusetts Commission of Mental Diseases succeeded this board. This Commission is now the Department of Mental Diseases and is the present organization having general supervision of the mental health of the Commonwealth of Massachusetts. The Department of Mental Diseases is headed by a commissioner who is a full-time, paid officer of the Commonwealth with three associate commissioners who are unpaid and who serve in an advisory capacity. The first Commissioner of Mental Diseases was the late George M. Kline, formerly president of The American Psychiatric Association, who served as Commissioner until his untimely death in January, 1933.

It is to the credit of Massachusetts that this position is considered nonpolitical; thus Dr. Kline was originally appointed by a Republican governor and re-appointed by a Democrat. His successor, Dr. James V. May, the present President of the American Psychiatric Association, was appointed without any political consideration because of his outstanding position in psychiatry. Nothing can be more important for the welfare of psychiatric work in the Commonwealth than the continuation of this tradition.

The duties of the Department of Mental Diseases of the Commonwealth of Massachusetts are outlined in the annual report of the Commissioner for 1931 as follows:

> The Department has general supervision of all public and private institutions for the mentally ill, feebleminded, epileptic and for persons in private hospitals addicted to the intemperate use of narcotics and stimulants. It has the right to make investigations and recommendations as to any matter relating to the classes under care, but the local administration of each state institu-

tion, however, is under the control of its own Board of Trustees appointed by the Governor and Council.

The direct powers of the Department concern the interrelations of institutions and matters which are common to them all, such as the distribution and transfers of patients between them, deportation of patients to other states and countries, claim to support as state charges in institutions, etc.

The work of construction under special appropriations for new buildings and unusual repairs is under the control of the department, and also expenditures of money for such purposes. The Department is required to prepare plans for buildings and also to select land to be taken by the Commonwealth for new or existing institutions.

All requirements for maintenance appropriations are analyzed by the Department.

This quotation gives, however, only an inadequate index of the effect of the Department of Mental Diseases. Not only are the individual hospitals given much help in various administrative details, but the whole morale of the system is improved by the efforts of the Department to foster scientific investigation and treatment and to set up certain standards which it expects the various institutions to reach or surpass. A pathologist is maintained by the Department whose duty it is to investigate the sudden and unexpected deaths as well as to give assistance to the pathologists in the several state hospitals and to fill in when any hospital is without a pathologist.

The Department emphasizes the importance of extra mural services. Among those which it has fostered are the examination and treatment of individuals who have not reached a stage of mental disorder where hospitalization is required. To this end it has aided in the development of out-patient clinics in various communities throughout the Commonwealth, the staffs of the clinics being supplied in large part by the hospital serving that particular section of the state. In the course of time, the Department developed a special Division of Mental Hygiene which continued to stimulate the development of these clinics.

One of the most important aspects of the work of the Division of Mental Hygiene has been the establishment and maintenance of clinics devoted to the habit training of young children. The staff of the Division, consisting of psychiatrists, psychologists, and psychiatric social workers, in addition to work in the clinics, co-operates in educational programs which include the parent institute Univer-

sity Extension course, the Massachusetts Department of Public Health, Parent Teacher Associations, mothers' clubs, women's clubs, and the like. In addition, the Division of Mental Hygiene fosters investigative work in problems of psychiatry by supplying financial assistance for such work at several of the hospitals.

Another function carried on by the Department of Mental Diseases is the psychiatric examination of prisoners. Under the provisions of Section 100A, Chapter 123, General Laws (frequently referred to as the Briggs Law) the probation officer is required to notify the Clerk of the Court if a defendant, indicted or bound over, has been indicted more than once, or previously convicted of a felony. The clerk then notifies the Department which is directed to cause the person to be examined " with a view to determine the mental condition and the existence of any mental disease or defect which would affect his criminal responsibility." All persons indicted for a capital offense are reported regardless of previous record. A special Division of Examination of Prisoners has been created by the Department of Mental Diseases to carry on this work.

The implications of such a psychiatric review of prisoners must be quite obvious. In the course of several years, enormous quantities of information concerning the type of individuals coming before the courts has been acquired, and is being acquired. Furthermore, this type of examination has greatly reduced the frequency with which psychiatrists are employed as experts by both prosecution and defense to appear with differing opinions as to the sanity of a prisoner.

There is also a provision in the laws of the Commonwealth whereby the judge of any court of the Commonwealth may request the Department to assign a member of the state hospital staff to make such examination as he may deem necessary for the purpose of determining the mental condition of any person coming before the court; this statute has been interpreted as being applicable to both civil and criminal cases.

The Department also maintains a Division of Mental Deficiency. This Division has supervision of 15 travelling psychiatric school clinics. According to statute, the school committee of every town is required to furnish annually, under regulations prescribed by the Departments of Education and Mental Diseases, the names of chil-

dren three years or more retarded in mental development in attendance upon its public schools or of school age and resident therein. These children are referred for psychiatric examination. The school authorities may also request the examination of other children who, for one reason or another, are not satisfactorily adjusted in the school. Each of the state hospitals and state schools, with exception of the State Hospital for Epileptics, maintains a travelling psychiatric school clinic, consisting of a psychiatrist, psychologist, and psychiatric social worker.

The Massachusetts School Clinic system is the outgrowth of the experiment of the late Dr. Walter E. Fernald, who sent out a travelling clinic from the Waverly School in 1914. From 1915, through 1931, 57,644 children had been examined by these travelling clinics and in the year 1931, 6439 children submitted to such examinations.

The Division of Mental Deficiency is also interested in the community supervision of the feebleminded, in investigating the needs of both the community and the defectives, and in planning for the future care of mentally retarded individuals.

A Division of Social Service is maintained by the Department of Mental Diseases. This Division not only offers help and formulates standards for the social workers in the various institutions under the direction of the Department but also has direct supervision of the social workers connected with the Divisions for examination of prisoners, mental deficiency, and mental hygiene. This Division has done much to improve the standards of psychiatric social work and to increase the utilization of qualified workers in the state institutions. The Department also maintains Divisions of Statistical Research and of Statistics. These Departments are making a careful analysis of the various factors involved in the proper care of persons with mental disease and deficiency. One need not refer to a variety of other functions such as maintenance, support, construction, or of the work done by engineers, farm experts, and the like. Suffice it to say that the Department aids the various hospitals for mental disease and defect in a variety of ways.

Despite the supervision and aid given by the Department of Mental Diseases, the several hospitals and schools have a great degree of autonomy.

The following is a list of Massachusetts state hospitals arranged according to the year in which they opened:

Worcester State Hospital	1833
Boston State Hospital	1839
* Walter E. Fernald State School	1848
Taunton State Hospital	1854
Northampton State Hospital	1858
† Grafton State Hospital	1877
Danvers State Hospital	1878
Westborough State Hospital	1886
‡ Bridgewater State Hospital (Criminal Insane)	1886
§ Foxborough State Hospital	1893
Medfield State Hospital	1896
Monson State Hospital	1898
Gardner State Colony	1902
Wrentham State School	1907
‖ Boston Psychopathic Hospital	1912
Belchertown State School	1922
Metropolitan State Hospital	1930

* Formerly known as the Massachusetts School for the Feebleminded.

† Formerly known as the Worcester State Asylum. The name was changed in 1915 to the Grafton State Hospital. In 1919, the original building of the Worcester State Asylum—at Summer Street—became a part of the Worcester State Hospital.

‡ The Department supervises the mentally ill at this institution which is under the Department of Correction.

§ Originally opened as a hospital for dipsomaniacs and inebriates. First insane patients received 1905. Devoted exclusively to the care of the insane since 1914.

‖ The Psychopathic Hospital was first opened as a part of the Boston State Hospital in 1912, and is now known as the Boston Psychopathic Hospital. In 1920 it became a separate institution with its own Board of Trustees.

These hospitals are scattered throughout the State of Massachusetts so that each hospital serves a certain geographical division of the state.

Space does not permit a long account of the various institutions but a few words may not be out of place. The Worcester State Hospital, having the distinction of being the first state mental hospital in Massachusetts opened its doors in 1833. The original building is still being used, though somewhat distant from the present main hospital. The Worcester State Hospital prides itself on the fact that it was one of the early American institutions to stress

neuro-pathology, having erected a special laboratory building for pathological study; it also has justifiable pride in having attracted to the position of pathologist such men as Drs. Adolf Meyer and Samuel T. Orton, both of whom have served as presidents of the American Psychiatric Association. But Worcester State Hospital has not been satisfied to rest on its previous accomplishments and is now one of the most active mental hospitals in the country. Important research is being carried on in endocrinology, special funds having been obtained outside the state appropriation for this purpose. Having a special staff for child guidance problems, the hospital is also extremely active in community work, having developed a Child Guidance Clinic, which serves the Worcester district under hospital direction.

The Boston State Hospital originally opened its doors to patients in the autumn of 1839 as a City of Boston institution and was taken over by the state in 1908. It was built following an act of legislature passed in the year 1836 which made it imperative for the several counties of the Commonwealth to provide suitable accommodations for those persons within their limits who, being idiotic or incurably insane, were too unsafe to themselves or others to be allowed to go at large, and who, on account of the crowded condition of that institution, could not be received at the Lunatic Hospital at Worcester.

An excerpt from the "American Notes" by Charles Dickens in 1842 suggests that Boston State Hospital started off with the spirit that might well be called modern.

> Every patient in this asylum sits down to dinner every day with a knife and fork; and in the midst of them sits the gentleman whose manner of dealing with his charges I have just described. At every meal, moral influence alone restrains the more violent among them from cutting the throats of the rest; but the effect of that influence is reduced to an absolute certainty, and is found, even as a measure of restraint, to say nothing of it as a means of cure, a hundred times more efficacious than all the straight waistcoats, fetters, and handcuffs that ignorance, prejudice and cruelty have manufactured since the creation of the world.
>
> In the labor department every patient is as freely trusted with the tools of his trade as if he were a sane man. In the garden and on the farm they work with spades, rakes and hoes. For amusement they walk, run, fish, paint, read, and ride out to take the air in carriages provided for the purpose. They have among themselves a sewing society to make clothes for the poor, which holds meetings, passes resolutions, never comes to fisticuffs or bowie-knives

as sane assemblies have been known to do elsewhere; and conducts all its proceedings with the greatest decorum. The irritability which would otherwise be expended on their own flesh, clothes and furniture is dissipated in these pursuits. They are cheerful, tranquil and healthy.

It is obvious that one great feature of this system is the inculcation and encouragement, even among such unhappy persons, of a decent self-respect.

In the last fifteen years this hospital has been under the superintendency of Dr. James V. May, the present President of the American Psychiatric Association.

Among other noteworthy achievements of recent years, has been the development of a psychopathic department of this hospital and the furnishing of clinical facilities for the teaching of psychiatry at Tufts Medical School.

The Taunton State Hospital was opened in 1854, to care for the people in the southern part of Massachusetts and of the Cape Cod region. The Northampton State Hospital was opened in 1858 to serve the western part of the state. Both of these institutions have been the important psychiatric centers of a somewhat scattered and rural population. They have been outstanding as the psychiatric headquarters in their special locations. The Grafton Hospital, opened in 1877, is really an outgrowth of the Worcester State Hospital which may be said to have divided into two parts, the Grafton Hospital, for a number of years, devoting most of its attention to the care of chronic insane.

The Danvers State Hospital, opened in 1878, has already been mentioned because of the important psychiatric personnel that it has given to the country. Bearing this in mind, one can have no doubt as to the importance of this institution in the history of psychiatry in Massachusetts.

The Westborough State Hospital opened in 1886. It was organized for those individuals who desired homeopathic treatment. As the years have gone on, the name homeopathic has lost its sectarian significance. This hospital is always rated highly for its management, treatment, and modern attitude.

In 1898, the Monson State Hospital was organized for the care of epileptics. It is one of the few institutions in this country devoted entirely to this disorder.

The Gardner State Colony opened in 1902 and has been devoted largely to the care of chronic mental disorders in able-bodied indi-

viduals. Here has been developed an institution peculiarly fitted to make such individuals happy, self-respecting, and useful.

The Medfield State Hospital, organized in 1896, and the Foxboro State Hospital, which first received insane patients in 1905, have developed in much the same way as the other state institutions.

The Metropolitan State Hospital opened for the reception of patients in 1930. It is a culmination of a number of years of study on the part of the Department of Mental Diseases to develop a modern hospital for mental diseases. It is believed by many to be the last word in organization and facilities, combining efficiency and economy, beauty and serviceability.

The Walter E. Fernald State School, formerly known as the Massachusetts School for Feebleminded was opened in 1848. It unquestionably bears the impress of the man who did so much to make the care of the mentally defective what it is today; the Dr. Walter E. Fernald School carries on the ideals and methods of Dr. Fernald. It has stood as the model for the Wrentham State School, opened in 1897 and Belchertown State School, opened in 1922. To members of this Association it is needless to call attention to the many contributions of Dr. Fernald and the school bearing his name.

The Boston Psychopathic Hospital was opened in June 1912 as a Department of the Boston State Hospital. It was established by an act of legislature in 1909 "establishing in the City of Boston a hospital for the first care and observation of mental patients and the treatment of acute and curable mental diseases and for an out patient department, treatment rooms, and laboratories for scientific research as to the nature, causes and results of insanity."

In 1920, the Psychopathic Hospital was separated from the Boston State Hospital and made an independent unit. The hospital under the medical direction of Dr. E. E. Southard, tended from the outset to carry out the provisions of the enabling act and in its first year admitted over 1500 patients to its wards, most of whom were for brief observation, being either sent back to the community through the out-patient department, or to other state hospitals in the course of approximately ten days, while a small number of acute or presumably curable patients were kept for more continuous treatment. Many patients were sent by the courts, police officers and social agencies for consideration as to their sanity. The out-patient department opened promptly and its need was indicated by the fact

that in the first year 830 individuals sought help. In the second year 1133 patients were seen. Dr. Thom, a former chief of the out-patient department stated:

> The work in general in the out-patient department falls roughly into four classes:
>
> *First:* The out-patient medical, psychological and social examiners have to deal with questions of feeblemindedness and mental defect, especially in regard to the mentally defective delinquents referred from courts, reformatories or other institutions, including an increasing number of backward children from schools.
>
> *Second:* The out-patient department handles psychiatric cases, both patients discharged from the Psychopathic Hospital and from other state hospitals (those who have a residence in or near Boston who can most conveniently resort to the Psychopathic Hospital out-patient department). Also, there is a certain number of patients who have never been in a hospital, but still require treatment for mild or incipient mental troubles of a noncommittable nature.
>
> *Third:* The out-patient department handles a good many somatic cases, cases that require physical treatment of various sorts in connection with diseases of the nervous system. The largest class falling thereunder is that of the neurosyphilitics, a great number of whom are physically fit for ambulatory treatment.
>
> *Fourth:* There is a group of cases that are, more narrowly speaking, cases of the social service group, requiring aid chiefly from the community's point of view. We here deal with cases suffering from the effects, pre-eminently of poor housing, poverty, desertion, and the like, all of which evils are based upon or laid down upon the background of mental inadequacy.

Investigation of mental diseases from the clinical and laboratory aspects has been continuously prosecuted. Teaching is looked upon as an important and integral responsibility of the hospital, both from the standpoint of medical students and graduates in medicine. Psychiatric teaching at Harvard Medical School is carried on in the wards of the hospital, and lectures and clinics have been given to the other medical schools of Boston from time to time. Of particular significance was the development of psychiatric social work at this institution. The term psychiatric social work originated at the Boston Psychopathic Hospital, much of the impetus to this type of social work came from the concepts and formulations developed by its social service department and the first training school for psychiatric social work was a co-operative experiment of the hospital and Smith College. It may be stated also that the development of out-patient psychiatry in relation to the Massachusetts

state hospital system had its origin in the out-patient department of the Boston Psychopathic Hospital.

Since 1921, the direction of the medical work of the Psychopathic Hospital has been in charge of Dr. C. Macfie Campbell, who, as director of the Psychopathic Hospital, Professor of Psychiatry at the Harvard Medical School, and President of the Massachusetts Society for Mental Hygiene, has had a dominant rôle in the development of psychiatric thought in the community.

It has already been indicated that psychiatric interest in Massachusetts has gone outside the walls of the institutions and been turned to the problems of the community. A great force in this direction has been the Judge Baker Foundation, established in Boston in 1916, as a memorial to the late Judge Baker of the Juvenile Court.

The Directors of this Foundation are Drs. William J. Healy and Augusta Bronner who headed this work in the beginning and have continued with the Foundation to the present time. Originally established to aid the Judge of the Juvenile Court in the disposition and handling of the juvenile delinquents, the work of the Judge Baker Foundation has developed along the lines of juvenile guidance of both delinquents and non-delinquents. The work of Drs. Healey and Bronner in the study and treatment of juvenile problems has exerted its influence not only in Massachusetts, but throughout the country.

Animated by the same spirit of doing preventive work, the staff of the McLean Hospital has developed a psychiatric service in the wards and the out-patient department of the Massachusetts General Hospital.

At the Children's Hospital, a special department has been developed for the study of handicapped children, stressing the neurological and training techniques as applied to mentally and neurologically handicapped children.

The Massachusetts Society for Mental Hygiene has functioned as an agency for disseminating information concerning psychiatric problems and mental hygiene through lectures, consultation service and stimulation of clinics. It has interested itself in the problem of mental hygiene in industry and stimulated interest among social agencies.

That the ideas of mental hygiene have infiltrated the community is well exemplified by a number of social agencies having psychiatric social workers attached to their staffs and by the use that many of the social agencies make of the psychiatric out-patient departments, the Judge Baker Foundation, and the Habit Clinics. It has already been noted that the school system of the Commonwealth has co-operated with the Department of Mental Diseases in the examination of certain pupils in the system. Likewise, the correctional system of the Commonwealth has not been unmindful of psychiatric problems. At the Concord Reformatory for Men, a psychiatrist has been on duty for many years. At the Bridgewater State Hospital, under the Department of Correction, there has been developed a Department for Defective Delinquents. Historically this Department is the second one to be developed in the country. At Framingham Reformatory for Women a psychiatrist makes visits at stated intervals. At the Lyman Reform School, a psychiatrist is in residence.

It is of significance that a psychiatrist of note and a member of the Association, Dr. A. Warren Stearns, who was Commissioner of Correction for the Commonwealth until he resigned last year, states:

> I began doing something which was called psychiatry at the Charlestown State Prison in 1915. This has now developed into a rather comprehensive case study of each admission. Perhaps the most important thing, though it does not directly involve psychiatry, but may be well thought of as a development of psychiatry, was the establishing by the legislature last year, of the Division of Research for the Prevention of Crime.

There is appended a list of the private licensed hospitals for mental diseases in Massachusetts:

For the Care of Mental and Nervous Diseases.

Bournewood, George H. Torney, M. D., 300 South Street, Brookline.
Channing Sanitarium, Donald Gregg, M. D., Wellesley Avenue, Wellesley.
The Reeves Sanitarium, Fred B. Jewett, M. D., 283 Vinton Street, Melrose Highlands.
Glenside, Mabel D. Ordway, M. D., 6 Parley Vale, Jamaica Plain.
Herbert Hall Hospital, Walter C. Haviland, M. D., 223 Salisbury Street, Worcester.
McLean Hospital: For nervous and mental patients (opened 1818): Department of Massachusetts General Hospital Corporation, Waverly. Honorary President: Henry P. Walcott, M. D., Cambridge.
Westwood Lodge, William J. Hammond, M. D., Westwood.
Wiswall Sanatorium, Inc., Harry O. Spalding, M. D., 203 Grove Street, Wellesley.

FOR THE CARE OF PERSONS ADDICTED TO THE INTEMPERATE USE OF NARCOTICS OR STIMULANTS.

Private Hospital, Frederick L. Taylor, M. D., 45 Center Street, Roxbury.

Washingtonian Home, Hugh Barr Gray, M. D., 41 Waltham Street, Boston.

FOR THE CARE OF MENTAL DEFECTIVES.

Woodlawn Sanatorium, Dr. Ewan A. Robertson, 500 Crafts Street, West Newton.

THE EFFECT OF THE ADMINISTRATION OF SODIUM AMYTAL AND SODIUM RHODANATE ON MENTAL PATIENTS.*

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Sodium Amytal.

The therapeutic effects of the barbituric acid derivatives were first demonstrated by E. Fischer and J. von Mering [1] in 1903 and since then a large number of derivatives have been introduced in the pharmacopeia. One of these derivatives is amytal (iso-amyl-ethyl barbituric acid) which complies in its chemical structure with the essentials which Fischer demonstrated, at that time, were necessary to obtain an hypnotic effect.

This substance was prepared by Shonle and Moment,[2] in 1923, and used in the form of its sodium salt for injection to produce anæsthesia in experimental animals and more recently various clinical studies have been carried out.[3] Some of the physiological responses under its influence, have also been carefully studied.[4] It is unnecessary at this time to go into an extensive discussion of these studies except to point out that Page and Coryllos [5] found that the average minimum effective anæsthetic dose was 35 mg. per kg. in the dog when given intravenously. Swanson found that in the routine intravenous administration of the salt for the production of anæsthesia in animals about 45 to 60 mg. per kg. were necessary before actual operative procedures could be carried out.

In man it was found that with 3 to 6 mg. per kg. the sensorium was mildly depressed and the patient did not lose consciousness as a rule, but slept at intervals; and with 15 to 25 mg. per kg., intravenously, surgical anæsthesia usually was produced. Man thus appeared somewhat more susceptible to the drug than the dog since he required only one-third to one-half the amount to produce surgi-

* Read at the eighty-eighth annual meeting of The American Psychiatric Association, Philadelphia, Pa., May 30–June 3, 1932.

cal anæsthesia.[6] Jackson [7] showed that man was also more susceptible to the hypnotic effects of iso-propylethyl barbituric acid, a very closely related compound, and suggested that "the higher psychic centers of man's cerebrum" probably accounted for its increased susceptibility over that of the dog. This however is pure speculation. It has been shown, for example, that in the same colony of rats, diet, season of the year, temperature of the quarters in which the animals are kept may considerably influence the "minimal effective dose" and the minimal lethal dose of hypnotics. Such factors may also account for some of the variations observed clinically.

Fitch, Waters and Tatum [8] who have been investigating the barbituric acid derivatives point out that marked variability in pharmacological activity results from only small changes in chemical structure; thus toxicity, rate of elimination, duration of action and other physiological effects may be markedly influenced. The choice of the barbituric acid derivative is therefore of some importance for the result which one may wish to obtain.

Owing to the physiological disturbances in the vegetative sphere observed in mental patients we were interested in studying, in a comparative way, the physiological responses of such patients under the influence of the barbituric acid derivatives which have a predelection for the brain stem, particularly the thalamic region, as had been shown by Keeser, Pick and others.[9] We shall not go into any detail regarding this phase of the work, which will be reported later, and only consider the effect on the mental state. Our interest was drawn to amytal particularly in this connection as a result of the report by Lorenz,[10] which was confirmed by Solomon and his coworkers,[11] that following a period of narcosis with sodium amytal cases of catatonic stupor may develop, temporarily, a lucid interval and also the favorable reports by Bleckwenn [12] of its use in neuropsychiatric conditions.

PROCEDURE.

A group of 17 patients, with varying psychopathological manifestations (manic-depressive psychoses, manic and depressed phases, dementia præcox, psychoneuroses, mixed types) were studied in the following manner. The studies were carried out in the morning, no breakfast being given. The sodium amytal * was dissolved in sterile

* We are indebted to the Eli Lilly Company for a supply of sodium amytal for intravenous use for this study.

distilled water forming a 10 per cent solution. This was prepared immediately before injection in order to avoid any deterioration of the solution and was injected intravenously at the rate of 1 cc. per minute. Following each half cubic centimeter the patient was questioned in order to note the effect of the drug upon the mental state. When any change was observed the injection was temporarily stopped and the patient questioned for a short period to ascertain the nature of this change. The injection usually was continued until 0.5 to 1.0 gm. of sodium amytal was administered and narcosis induced. At a subsequent period these patients were put upon sodium amytal orally in doses from gr. III b. i. d. to t. i. d. for a variable period of time for comparative study.

OBSERVATIONS.

A small group of patients with various types of psychoses was encountered who presented exceedingly interesting ameliorating effects from the administration of only 1 to 1.5 cc. of the solution (equivalent to 100 to 150 mg.) intravenously. Several of these patients stated that they felt they had returned to a normal condition. In some of the cases the marked changes occurred within 15 seconds to 30 seconds following the completion of the injection of 1 cc. This effect was not necessarily accompanied by any sign of drowsiness, the patient responding readily to questions and maintaining a sustained conversation. The improvement was usually more marked at this time before narcosis was induced than that seen after the patient was aroused from a narcosis which was usually one hour after completion of the injection.

Another group of patients became more communicative as a result of the injection, before an amount sufficient to produce narcosis was given. However, their mental content and general trend remained unchanged. Some patients showed no notable change, either remaining mute or answering in their usual manner.

The oral mode of administration, however, did not produce, at any time, such marked ameliorating effects upon the psychopathological manifestations as did the small intravenous injection in the first group described. Some of the patients, however, became more amenable to treatment, although still presenting a definite pathological picture, others remained unchanged.

The results obtained with sodium amytal as contrasted with the effects produced by sodium rhodanate will be taken up subsequently in the section dealing with the latter.

The following are a few of the protocols illustrating some of the ameliorating effects of the intravenous injection of sodium amytal without narcosis.

1. N. M., female, Age 19. Wt. 43.8 kg. Diagnosis: Manic-depressive psychosis.

Patient displayed mannerisms and spoke irrelevantly. Within 45 seconds following the intravenous injection of 1 cc. of 10 per cent sodium amytal, she became oriented and held conversation with the doctor for about 20 minutes. After about one hour she had a prolonged crying spell. On two previous occasions, injections of sodium amytal failed to produce this temporary ameliorating effect.

2. C. N., female, Age 30. Weight 50.5 kg. Diagnosis: Dementia præcox.

Agitated, crying, complaining of thoughts continually running through her head.

Following 1 cc. of a 10 per cent solution of sodium amytal intravenously, the patient felt better immediately. Stated that the flow of thoughts had stopped and that she would be quite well if this state would continue.

3. A. S., male, Age 32. Weight 82 kg. Diagnosis: Manic-depressive psychosis.

Patient was agitated, complaining that he was suffering from a "mental strain." Within two minutes following the intravenous injection of 1 cc. of sodium amytal, the patient stated that he felt like himself again.

He was given another cubic centimeter of sodium amytal, following which the patient smiled, and stated that he felt as if he had been "lifted out" of his sickness.

4. P. B., male, Age 16. Weight 54 Kg. Diagnosis: Manic-depressive psychosis.

Agitated, impulsive, shouting, "I want my freedom," "I am upset," etc. One cubic centimeter of sodium amytal (10 per cent solution injected) intravenously. One minute later, patient said, "I feels more in my normal senses," . . . . "more myself."

DISCUSSION.

Lindermann[13] reported that 3 to 4½ grains (180 to 270 mg.) of sodium amytal intravenously removed the mental tension of patients and rendered them communicative so that they related things pertaining to personal matters which they really did not desire to do. This effect he claimed also occurred in normal individuals.

However, one of our cases, diagnosed as manic depressive, depressed, came out of a stupor, was alert, facetious, interested in various tests which were being performed at the time, asked questions about them but said she refused to relate anything pertaining to herself. Another patient of the schizophrenic group was quite communicative before the hypnotic was administered and refused to tell of her personal problems either while the hypnotic was being administered or following narcosis which lasted about one hour. When she was aroused, she refused to discuss personal matters and only on questioning and reassurance that the matter would not be discussed with anyone she stated that the injection of the drug had produced erotic feelings.

Our findings are in agreement with those of Lindermann that narcosis is not necessary in certain cases to remove psychopathological manifestations.

Lorenz [10] who was associated with the late Dr. Lovenhart in demonstrating the remarkable effects of high carbon dioxide and oxygen inhalations and also of cyanide injections upon certain catatonic stupors, states that the effects of sodium amytal in such cases cannot be explained upon the same basis, namely, as due to an effect upon oxygen metabolism. He believes that amytal works by "producing a state of unconsciousness so profound as to dislodge the mental mechanism responsible for the catatonic stupor." Bleckwenn,[11] however, reported a few cases receiving hypnotic doses of amytal in which a lucid interval occurred for a few minutes before they became unconscious. During this short period the patients were rational and had complete insight. As we have indicated, a state of unconsciousness has not been found necessary to produce marked ameliorating effects in certain other psychiatric cases. It is difficult to understand why physico-chemical explanations should be applied to the action of the high CO_2 inhalations and cyanide injections and psychological explanations for the effect produced by sodium amytal. We must admit our ignorance, as yet, regarding the mechanisms involved in either case.

Our personal experience with prolonged narcosis has been limited because of the risk involved in such therapy.

Although the literature contains reports of excitement and aggravation of symptoms in certain cases receiving sodium amytal, no such manifestations were observed in the cases which we studied.

Sodium Rhodanate.

The next phase of the study was concerned with observations regarding the action of sodium rhodanate as compared with that of sodium amytal in the same mental patients.

In 1903, Pauli [15] reported that sodium rhodanate had a sedative or quieting effect upon the anxiety and agitation of patients suffering from neurosis and nervous conditions associated with organic disease. He based his therapy upon the working hypothesis that the nervous conditions might possibly be due to disturbance in the colloidal or physical state of the protoplasm in the nerve-cell which he sought to alter by the administration of rhodanate. The reason the rhodanate was chosen by him was that *in vitro* experiments with protein solutions indicated that the rhodanate ions (CNS) had a marked antagonistic action to the coagulating or aggregating effect of various cations. Pauli pointed out that this working hypothesis was based merely upon analogy. No proof was offered that the therapeutic effects were produced through changes in the colloidal state in the patients treated.

In 1912, G. Marinesco [16] studied fresh nerve-cell preparations with the aid of the ultramicroscope and demonstrated that certain agents either physical or chemical brought about in the cells, changes of either an increased granular appearance or a clearing of the cell contents. This was interpreted as either coagulation or liquifaction of the protoplasm. These were all *in vitro* experiments and did not demonstrate that similar changes were produced in the living animal by doses of the reagents producing physiological effects. Furthermore even if such changes had been demonstrated in the cells of the nervous system of the intact animal they still might not necessarily be the cause for the physiological effects produced by these agents. It is not intended by this view to minimize the importance of the physical state upon physico-chemical reaction, surface chemistry, etc.

Haldi [17] and his coworkers demonstrated that various parts of the brain differed in the extent of swelling when placed in the same solution. They also showed that the inhibitory effect of certain ions upon swelling of the tissues in distilled water was different for different parts of the brain and they postulated that this relative difference of various parts of the brain to the specific ionic effects upon hydration of the tissues may be the basis of various psychic dis-

orders and that ions present in the brain and blood were undoubtedly factors in physico-chemical regulation.

Ludlum and Taft [18] on the basis of physico-chemical studies of the serum of mental patients expressed the opinion that a correlation exists between the colloidal character of the tissues of the brain and mental states, including the velocity of physico-chemical reactions and psychic action.

In 1930, Ludlum and his coworkers [19] reported some observation on the histology of the nervous system with the ultramicroscope and discussed the importance of the colloidal state and water for the physiology of the nervous system. They pointed out however that ions have other effects besides simple swelling and hydration which are important considerations in physiology.

Recently, Bancroft [20] and his coworkers have stated: "From the literature it is evident that there are two general types of insanity, one in which the brain-colloids are slightly over-coagulated or puckered, and the other in which the brain-colloids are slightly over-peptized or mushy." They suggested that tests be carried out on mental patients with what they called coagulating agents and peptizing agents in an attempt to correct the abnormal colloidal state. They recommended sodium amytal as the coagulating agent and sodium rhodanate as the peptizing agent.

Such tests were carried out by Lang and Patterson [21] at the suggestion of Bancroft. They concluded: "This study has demonstrated definitely that the functional psychoses show a correlation between the syndromes presented and the state of dispersion of the cell-colloids."

It was not evident to us from the review of the literature presented by Bancroft that two general types of insanity existed depending upon the colloidal state of the brain nor could we ascertain from the study of Lang and Patterson that the evidence which they presented in any way indicated the state of dispersion of the cell-colloids even though, as they claimed, there was a correlation between the syndrome presented and the reaction to the drugs used. Furthermore, Lang and Patterson speak of mixed syndromes. It is difficult to see how they can accept dispersion or agglomeration of the brain as the two opposing colloidal states which determine the nature of the mental aberration and then speak of mixed syndromes,

for, it would require that the brain be both agglomerated and dispersed at the same time.

Although we were not inclined to accept the physico-chemical explanations offered, it did not preclude the possibility that the two drugs had opposing and discriminating effects. Since we were engaged in a study of the action of sodium amytal at the time of Bancroft's report as indicated earlier in the paper, we extended the study to obtain information regarding the comparative action of sodium rhodanate.

PROCEDURE.

Sodium rhodanate was administered to a group of patients by a method similar to that recommended by Lang and Patterson. Five grains of sodium rhodanate (Merck's C. P.) dissolved in a small amount of water was given together with 5 grains of sodium bicarbonate b. i. d., after meals. The dose was increased 5 grains daily. The maximum dose per day was 30 grains administered usually in 10 grain doses t. i. d. and then in 15 grain doses b. i. d. The patient was kept on this dose for a variable period of time and the effects recorded. Several of the patients developed toxic manifestations during the administration of the drug so that it had to be discontinued. The blood pressures were recorded and blood counts were taken at varying intervals.

Following a period of observation on sodium rhodanate a rest period of a few days was allowed and then sodium amytal was given orally, starting with grains III b. i. d. to t. i. d. (in a few cases the dose was increased above this point). In some patients sodium amytal was administered first and was then followed by a period of sodium rhodanate.

RESULTS.

In the entire group studied, sodium rhodanate did not appear to produce any noticeable ameliorating effects during the period of administration.

In some, definite toxic manifestations occurred. Two patients (Mr. P. B. and Mrs. K. R.) developed diffuse macular eruptions covering the entire trunk and extremities together with a diffuse erythema of the face which was followed by a brany desquamation of the skin in one of the cases.[22] The eruption was associated with a febrile reaction in both cases.

In one of these cases the dose had reached grains 10 t. i. d. and had been maintained at this level for 5 days and in the other the dose reached was 30 grains a day which had been administered for two days. No appreciable change in the mental picture was noted during the period of administration of the rhodanate to these patients.

Another case (Mrs. I. B.) diagnosed as psychoneurosis, conversion hysteria, who had been on sodium rhodanate gr. XV b. i. d. for 20 days suddenly developed a stupor accompanied by fever. A blood count also revealed a marked secondary anemia. Examination of the spinal fluid was negative. Following two days of stupor she gradually regained consciousness and from then on continued to improve steadily. We cannot say what causal relation, if any, existed between the stupor, fever, and recovery.

Several of the patients lost weight when the sodium rhodanate was started but this was not a constant feature nor was it progressive during the period of rhodanate administration, when it occurred. Some complained of nausea during the first few days of sodium rhodanate administration.

We were not aware of any unusual aggravation of the mental symptoms during the administration of the rhodanate except the case of stupor previously described and that of a young male patient, diagnosed as a manic depressive, manic. This patient's agitation was markedly increased. After sodium rhodanate was discontinued the aggravated state continued for several days and the patient then gradually began to show some signs of change towards the manic status presented before the administration of the rhodanate.

In the cases which were studied, sodium rhodanate failed to produce any noticeable therapeutic effect during the period of administration nor could we ascertain any effect of sodium rhodanate which could be used as a diagnostic aid in mental diseases.*

The chart represents in graphic form the impression of the sum total produced by the oral administration of sodium amytal effect

* As this paper was being sent to press, a paper by H. D. Palmer and A. L. Paine, Prolonged Narcosis as Therapy in the Psychoses, Amer. J. Psychiatry xii, p. 143 (1932), appeared, in which they indicated that the greatest success which they obtained with sodium amytal was in the group of manic-depressive psychosis contrary to the claims of Bancroft and his coworkers and Lang and Patterson.

THE EFFECTS OF AMYTAL AND RHODANATE MEDICATION

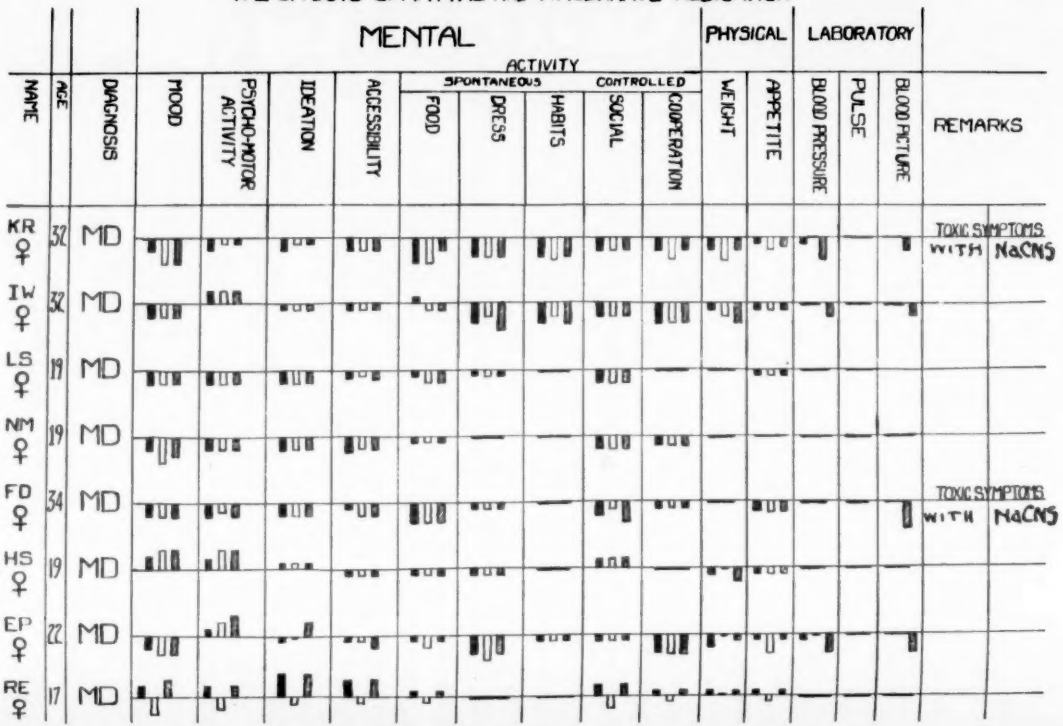

CHART I.

THE EFFECTS OF AMYTAL AND RHODANATE MEDICATION (CONTINUED)

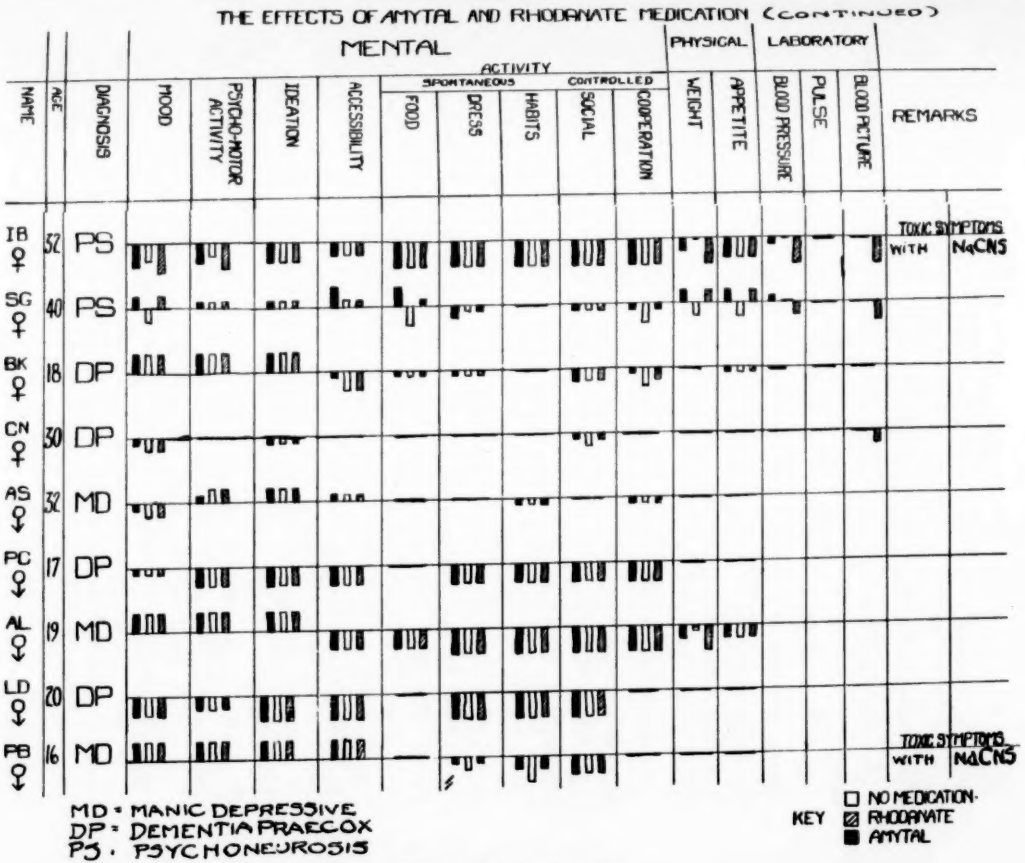

CHART I (Continued).

and sodium rhodanate in various patients. The blocked areas above the base line indicate states elevated above normal and those below the line indicate depressed states.

CONCLUSION.

1. Sodium amytal, intravenously, may produce marked, transient ameliorating effects in some psychotic patients.

2. The temporary improvement with sodium amytal seen in some cases occurred without the induction of narcosis.

3. The oral administration of sodium amytal, even in hypnotic doses, was not as effective as the intravenous in producing the transient ameliorating manifestations seen in some of the patients.

4. Sodium rhodanate was without any noticeable therapeutic effect in the cases studied.

5. Some toxic manifestations were observed in several cases following the oral administration of sodium rhodanate.

6. No contrasting effects were observed between sodium amytal and sodium rhodanate which could be of diagnositic value.

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DISCUSSION.

KARL H. LANGENSTRASS (Washington, D. C.).—I am sure we all appreciate greatly the work done by Drs. Harris and Katz, and have much enjoyed their presentation. Dr. Freeman had planned to open this discussion. However, he is unable to be with us today; so I have been asked to say a few words in his place.

The last two years have witnessed the publication of a series of papers in the Proceedings of the National Academy of Sciences and in the Journal of Physical Chemistry. Written by Professor Bancroft of Cornell University and his coworkers, these papers propose to shed some new light on such vital neuropsychiatric problems as: Surgical anesthesia, drug addiction and functional psychosis. It may justly be regretted that the program of this meeting does not include presentations of favorable experiences with the clinical application of Bancroft's ideas and theories. The report that we have just heard affords a welcome opportunity to consider these ideas here. May I, therefore, suggest that this discussion be extended from the deliberation on Drs. Harris' and Katz's report to that of Bancroft's recent publications, so far as they are of psychiatric interest. I feel that we have every reason to be thankful, if a man of Professor Bancroft's standing is willing to devote his time, his skill as an experimenter and his scientific endowment to problems in our particular field. We ask: What has he to say, and what do his statements mean to us as psychiatrists?

More than 70 years back, in 1860, the German pharmacologist, Binz, formulated the hypothesis: *Surgical anesthesia is a reversible coagulation of brain-cells.*

He was able to show experimentally that dilute solutions of morphine have a coagulating effect on brain tissue and further that this coagulation is reversible. In 1875, the French physiologist, Claude Bernard, published a series of lectures on surgical anesthesia. He accepted the theory of Binz. The following sentences from Claude Bernard's book elucidate the situation:

"Anesthetic drugs exert a physico-chemical action upon the nerve-cells. This consists in a semi-coagulation of their plasma. But this coagulation is not permanent. The nerve plasma can return to its normal state upon elimination of the toxic agent."

Bancroft's recent studies proceeded from this point. He applied his knowledge of modern colloid chemistry to the Bernard-Binz theory, and carried out extensive tests to prove its validity. He reached the conclusion that anesthesia or narcosis is indeed caused by reversible coagulation of the brain-cell colloids, and that the more recently formulated Meyer and Overton theory of anesthesia must be abandoned. Details of this very interesting and valuable work are found in contributions to the National Academy of Sciences and to the Journal of Physical Chemistry, of which Dr. Bancroft is the editor-in-chief. This part of Dr. Bancroft's work rests on solid ground. The theory is clearly not his. He states many times that he is elaborating and verifying the thesis of Bernard and Binz. But our author has translated it into the language of modern physical chemistry, and he has furthermore supported and surrounded it with extensive experimental evidence.

Morphine was used 70 years ago by Binz to produce reversible coagulation of brain tissue. Recently Bancroft experimented with dogs that he gradually accustomed and addicted to morphine. Withdrawal of the narcotic drug produced in these animals quite intense withdrawal symptoms, as we know them from human cases. Morphine, being a definite coagulating or agglomerating agent, the experimenter tried out the effect of a dispersing agent during the withdrawal period. He found, in accordance with his expectations and his theory, that the dogs tolerated the withdrawal of morphine easily if a dispersing agent was administered along with the decreasing doses of the narcotic drug. Bancroft used sodium thiocyanate (or sodium rhodanate, as he calls it) as the dispersing agent. This drug was chosen because it has an optimal dispersing effect on proteins in alkaline solution. It stands in this respect at the head of the lyotropic series of anions. This experience with morphine-conditioned dogs led our author to suggest that sodium thiocyanate be tried out in cases of morphinism in human subjects. He emphasized, however, that established routine therapeutic measures would have to be employed along with the colloidal reagent.

The British medical literature, as far back as 1897, contains reports on the relief of withdrawal symptoms and relief of the craving for morphine by means of dispersant drugs. The author is Dr. McLeod. He used sodium bromide, which from a colloid chemical viewpoint is a near relative to the

thiocyanate. It stands quite close to it in the lyotropic series for proteins. Dr. McLeod did not prescribe it as a dispersing agent, but gave it on general principles to a patient suffering from an intractable headache. The patient happened to be a morphine addict. The bromide medication put him to sleep. When he awoke from that sleep, his headache was gone and relieved also was his intense desire for morphine. What is more, he remained free from his drug craving for a period of over three years, and was still free from it at the time of the report. Bancroft, Gutsell and Richter have furnished to the National Academy of Sciences a detailed report on the successful treatment of a human morphine addict by means of gradual withdrawal, supplemented by oral administration of the dispersing drug, sodium thiocyanate.

In June, 1931, following a brief preliminary report to the Academy, the paper entitled: "Colloid Chemistry of Insanity," was published by Bancroft and Richter. It represents the next step. The authors suggest that functional mental disorders may be correlated with an abnormal degree of dispersion of the nerve-colloids. The abnormality is conceived as representing either *in*creased or *de*creased dispersion. Sanity or mental health is thought to be associated with a normal degree of dispersion, while mental disease would occur with deviations from this normal in one direction or the other. Lest misunderstanding arise, we want to point out that Bancroft and Richter do not make any sweeping claims or statements in this respect. Here are their own words:

"We do not claim that colloid chemistry will explain all of the phenomena of mental disorders, or serve as an extensive basis. But it is not improbable that, when medical knowledge is supplemented with colloid chemistry, the medical research worker will be freed of some of the present difficulties in regard to the functional disorders."

And again:

"It is not improbable that in mental disorders, not directly traceable to any structural disturbance, the cause may be found in some variation from the normal state of the brain-colloids."

Prof. Bancroft and his coworkers then take one more step by suggesting that their working hypothesis be tested clinically as a means of diagnosis and as an adjuvant to therapy. They say:

"Disorders of over-dispersion may be benefitted by coagulating agents. Disorders of decreased dispersion would be improved by peptizing agents."

We have here the suggestion that the multiplicity and complexity of psychiatric diagnoses be dispensed with, at least for the time being. The individual is either sane or insane. If he happens to be of unsound mind, a "diagnosis *ex iuvantibus*" is made. He may suffer from over-dispersion. The ingestion of a coagulating agent will then have a beneficial effect. For this purpose sodium amytal is used. If the disorder is associated with decreased dispersion, a peptizing agent should be helpful. Here the sodium thiocyanate is suggested. This sounds like simplicity itself, and we are tempted to say with Mark Twain: "Interesting . . . . if true." In all fairness to Bancroft, we must however again point out that he realizes just as well as anybody else the infinite complexity of the problems involved. He

is indeed very far from claiming or even thinking that he has anything like solved the problem of functional mental diseases. Nor does he claim to have found a cure-all for any or all mental ills. His own words may show this:

"This is by no means an exhaustive treatment of the subject dealing with the effects of colloidal reagents on the nervous system. . . . . It is the hope of the authors, that this paper may in a small way, stimulate medical research workers to recognize that there is no sharp boundary between medicine and colloid chemistry, and that their researches are incomplete if they have not either included or excluded the variations of the tissue colloids in the pathological conditions."

The suggestions of Bancroft with regard to functional mental disorders have since been carried out in several places. Lang and Paterson reported last November to the Academy of Sciences their experiences. Forty-six patients, suffering from various functional mental disorders, were given the sodium salt of iso-amyl-ethyl-barbituric acid by mouth on five successive days. After several days' interval, they received sodium thiocyanate by mouth for five or six days. The results were: Schizoid conditions were improved by the agglomerating agent of the barbituric acid series. Cycloid conditions were favorably influenced by the thiocyanate, a dispersing agent. Lang and Paterson conclude, that cases of functional psychosis do show a correlation between their clinical symptoms and the state of dispersion of their brain-colloids.

Little wonder that negative results should also have been met with. The paper of Drs. Harris and Katz constitutes one example. In their experience colloidal reagents of the agglomerating and of the peptizing type did not seem to bear any relation to the type of psychosis. The number of patients tested by them is small: 17, as compared with 46 in the Lang-Paterson series. The toxic symptoms that they observed with the rhodanate may possibly have been due to impurity of the drug they used. I wonder whether such a possibility was considered and ruled out. Then there is also the possibility of a cumulative action. Our authors gave the thiocyanate for about four weeks. Lang and Paterson, I think, discontinued it after five or six days. Did our authors consult Bancroft or his associates regarding the negative results and the toxic manifestations? It would be very interesting to know what they have to say about this matter.

On the whole, the introduction of physical chemistry into psychiatry has just about started. Chemically speaking, the colloid-chemical aspect of mental disease seems to be "*in statu nascendi.*" Therefore we see vivid, high-tempered reactions, absence of clear definition and even here and there some bubbling over. The matter fails to meet with everybody's approval. Or should I say that it has almost nobody's approval? Bancroft and Richter, on the other hand, in spite of the title of their contribution, have not written "The colloid chemistry of insanity." They have hardly more than given a few colloid-chemical aspects of it. Their introduction of two standard types of mental disease (they speak of insanity C and D) appears to be a step in the wrong direction.

Much more work must and will be done in this new and difficult, but promising field. This will lead to modification and refinement of methods. It will also gradually bridge the gap between the great, possibly too great, simplicity of the chemical hypothesis with its insanity C and D on the one side, and the equally great and even appalling complexity of the psycho-biologic problems and manifestations on the other. Most of the functional psychoses are certainly not of the types C or D. They continue to occupy a place at the other end of our alphabet with many an X, Y, and Z, symbolizing the problematic and the unknown.

Dr. Meyer M. Harris (New York City).—I do not think anyone can question the importance of chemistry or physical chemistry for an understanding of the physiology of the central nervous system, nor did we intend to intimate that. In the paper that was read before the Interstate Hospital Conference at the Psychiatric Institute on April 20th of this year, the importance of the effect of the physical state upon chemical reactions was indicated.

As to the question of the number of cases that were studied, it is true that the number was small. However we included in this group only those cases which had received sodium amytal and sodium rhodanate for contrast. We had a large number of cases which had been under observation with amytal alone. A good many of them were cases of manic-depressive psychosis in some of which we had observed improvement under amytal while in others there was no change. Very seldom, as Dr. Katz indicated, did we find any aggravation of the clinical manifestations. This seemed to be in opposition to the views expressed regarding this type of psychosis as belonging to the group of so-called agglomerated states which were aggravated by the administration of an agglomerating agent. This was also true in some of the manic depressives which had sodium amytal intravenously. In one case there was an immediate improvement noticed within a few minutes.

Regarding the question of impurities as the possible cause of the toxicity of the drug, a chemically pure Merck's preparation was used. If some very toxic agent were included in the drug I should imagine there would have been more cases of toxicity observed. Furthermore, the toxic reactions which we had observed had been previously reported in the literature.

We felt that if the claims made regarding the dispersed and agglomerated states of the brain in psychoses and the effect of these agents upon such states are correct, then one should obtain in studying contrasting effects, even though the group were small, something a little more clear-cut than what we had observed.

Although the physical state of the protoplasm is important there certainly must be other mechanisms involved. As a matter of fact, Ludlum pointed out, and one might state here that Bancroft carried out his work at the suggestion of Ludlum, that the mechanisms involved were not entirely questions of degree of agglomeration, if at all. He pointed out that ions have other effects which may be quite as important in the resulting changes in function.

There are indications from studies with sodium amytal, on the point of localization of the drug in the brain, which are of considerable importance if one considers the interest which has been centered recently on the hypothalamic region. The sham rage reactions, for example, that Cannon produced in his decorticated animals with the thalamic region intact, point to the probable important rôle of this area for such manifestations. A drug acting selectively on such an area is, I think, a consideration of appreciable importance. The drug does not act diffusely through the brain.

It seems to be rather too simple to conceive of the change in the whole physical state of the brain as the basis for the psychoses. In a review of some of the literature it was pointed out that even in regard to the physical state the brain varies in its reactions in different portions.

I might repeat for emphasis again, that we realize the importance of physical and chemical states for the function of the brain. For example, all the recent interest in water metabolism in relation to the convulsive states obviously points to some such close relationship, although some of the things which have been observed even in this connection seem to indicate that it is not entirely water alone that is involved.

I think that although the physical and chemical states are important the tendency has been to overemphasize, and perhaps to create a wrong impression as regards the importance of the colloidal state, or what was really known regarding the colloidal state, and its relationship to the functions of the brain as indicated by these drugs.

VERIFICATION OF EMOTIONAL REGRESSION BY TESTS.

By MANDEL SHERMAN, M. D., Ph. D., and BLAKE CRIDER, M. A.,
University of Chicago.

Emotional regression is not a rare condition but seldom is it objectively verified by appropriate tests. This paper describes the behavior of a patient and the evidence of the various levels of regression.

The patient was a young married woman, age 20, who normally was impulsive, aggressive, egocentric, restless and constantly active. The restlessness was manifested through the constant chewing of her nails or the end of a pencil while reading. She appeared nervous and smoked 20 to 30 cigarettes daily, the larger number especially when not actively occupied. In school she was a non-conformist but her misdemeanors were of a harmless and fun-provoking sort. She was insistent on an immediate gratification of her whims and frequently reacted angrily if one did not cater to her desires. In spite of her egocentricity she frequently had periods of depression. Although she was impulsive and often behaved in a manner not relished by others she made friends easily and quickly and was popular with both sexes.

She was placed in an orphanage by her parents during her first year and was adopted by a farmer and his wife when she was 16 months old.

After short acquaintance it was discovered that she lied frequently and with no apparent end in view. She told one story of having been in a serious automobile accident where her companion was killed. Another story was about a trip to New York City and of the many exciting adventures she had there. She reported receiving a scholarship for excellency of work in high school and of attending a local college. She frequently told of a certain "old woman" from the orphanage who appears suddenly, at dances, or at her back door, or on the street, whose purpose was to investigate for the orphanage her behavior and activities. These and many

other stories were proven to be untrue. On one occasion she told about drawing the cartoons for the high school year-book and brought the book as evidence of her statements. The real artist, however, had placed his own name on all cartoons.

According to her story, which has been verified, her foster mother was cruel to her but her foster father was very kind. At one time she was severely punished because she failed to set the table properly. At another time she was kicked vigorously because she forgot to feed the chickens. Sometimes she was hit on the head, struck across the back with a broom handle, or frequently slapped for minor misbehavior. As a result of these cruelties she attempted to hang herself when she was in the grade school but was discovered by her foster mother before she was able to carry out her plan.

At the age of 12 she was informed by one of her school chums that she was an an adopted daughter, which her foster parents denied, but in such a manner as to increase the conflict. She became extremely curious to find out who her real parents were. One aunt told her that her foster father was her real father and that she was the illegitimate daughter of a woman who was pointed out to her on the street. At 15 gossip among the neighbors was that she was pregnant and as a result she was ignored at all social functions. Nevertheless, she persisted in attending as many social functions as she could in order to show the gossipers that she was not concerned in the least, although she was greatly depressed. She attended the high school near her own home and supported herself by working as a maid in a rich family. As a result she felt keenly her economic and social inferiority to her school companions.

At 19 she married a man whom she met on a visit to a nearby city. She was not in love with him but merely was anxious to escape her home environment and live in the city. During the 10 months of marriage she carried on several extra-marital sexual affairs which she justified by the claim that her husband was cruel, negligent, and unfaithful to her. She finally left him because of his conduct towards her. There was apparently no sexual experience previous to her marriage. Her best girl friend and a large proportion of her foster relatives were thought of as serious social problems by the neighbors. She was well informed of the details of a foster grandfather who was a combination blacksmith, minister, and drunkard

and who seduced his own niece when she was only 16; of an aunt who was finally forced to get married after numerous sexual escapades; of another aunt who was a mistress of a professional gambler; of a cousin who ran a house of prostitution; of another grandfather who was killed by his own son; and of her grandmother who was killed by a neighbor. Her foster mother did not have the best reputation and her foster father of whom she was very fond was reputed to be her actual father.

The first symptoms of her acute emotional upsets began to manifest themselves when she was in the sixth grade. At that time she felt severely depressed and cried a good deal. She told the teacher she was ill and consequently was sent home. When she was in the second year of high school she fainted while visiting in a neighbor's home. This lasted several hours and a physician who was called diagnosed a nervous breakdown. The first severe attack occurred after she had wrecked the family automobile in an accident. She and her companion were carried to the hospital where no injuries of consequence were found. She was sent home but the next morning awoke completely "paralyzed." She could neither see nor hear. She was given glucose by hypodermic injections for a period of about three weeks. After the local physician said he was unable to do anything for her, a chiropractor was called. At the end of three weeks she suddenly recovered and with the exception of being slightly emaciated was normal.

Some time after marriage and while entertaining friends of her husband she suddenly fell in a faint on the floor. A physician diagnosed the trouble as epilepsy. This disturbance was characterized by a period of unconsciousness with the body periodically limp and rigid but without convulsions.

The more severe attacks and regression began to occur after a prolonged sleeping spell. One day she went to sleep at noon and slept until the afternoon of the next day. She awoke for a few minutes and went back to sleep. This lasted for about a week, with only occasional waking periods. Since then the attacks to be described have been occurring with increased frequency and severity. The attacks in most cases last only a few minutes and occur once or twice a week.

The first observation of a prolonged attack was made between 11 and 12 at night. The patient lost consciousness while rest-

ing on her bed. This period of unconsciousness shortly merged into a series of back and neck rigidities alternating with occasional periods of limpness of the entire body. During neither the quiescent nor the active state did the patient show any evidence of awareness of her surroundings. She was found to be insensible to the pricking of the skin with a needle. No amount of severe pinching of any part of the body succeeded in restoring her to consciousness. The pupillary and knee reflexes were present but no reaction could be elicited from stroking the bottom of her feet. There was an occasional twitching of the facial muscles, and of the fingers and hands. For a moment she apparently regained consciousness but immediately lapsed into unconsciousness. After a few minutes followed another series of alternating conscious and unconscious periods of one to three minutes each which lasted a total of 30 minutes. At times during this period her head and back were bent rigidly in a concave shape. At other times the body was completely limp. During rigidity she clenched her fists tightly, clawed at her throat, tore her clothes and strained as if in great agony. She frequently appeared to have great difficulty in swallowing and breathing. At the end of this 30-minute period she again became normal with the exception of an inability to see. During this period of blindness, which lasted about 20 minutes, the pupils reacted normally to light but she was unable to close her eyes. Approximately an hour after the beginning of the attack she was again completely oriented. Her only complaint was of fatigue and pains in the eyes. She was unable to recall anything that had occurred during the past hour.

This episode, obviously, contains many hysterical symptoms. On the subsequent night the regression phase was observed.

The patient lost consciousness while lying on the couch. As in the previous episode there was an alternation of conscious and unconscious periods of from one to three minutes each. In the majority of the unconscious periods she appeared to be delirious, clawed her throat, clothes, pillows or any available object. At the end of one of the active periods she calmed down, was quiet for a moment and was apparently normal again with the exception of being unable to see and to close her eyelids. She rubbed her eyes vigorously for a while and as if this lack of vision were the exciting cause, she again became extremely active and tossed about and tore at her clothes. After a few minutes of this behavior her activity subsided and she

seemed to be oriented but her personality seemed to change. There was a regression to a lower age level. In response to the question, "How old are you?" she answered, "I am two. No, I am six." Her behavior, however, was hardly beyond the three-year level. She said she had 16 fingers on one hand. She said she could not read or write but could draw pictures. When asked if she would draw a picture she answered in her own peculiar childish way, "I don't wanta." She did not recognize her own name, Mabel Ruth (the Ruth addition had been acquired at about 14 years of age). She was unable to recognize the names of any of her immediate friends. She had no conception of the meaning of the word, "Ohio," her native state. Of the Bible she said, "It is a funny thing." All of her conversation, manifestations, information, language, behavior, smiles were characteristic of a child of approximately three years of age. She spoke in the typical "baby talk." A cousin, very much older than the patient and who had known her as a child, said, "That is just the way she used to talk." Although she is an inveterate smoker she had not the least idea how to use a cigarette. The observer finally induced her, after much pleading, to attempt to write her name and draw a picture. She took the pencil in her left hand to write, relaxed suddenly and again lost consciousness. She recovered a moment later completely normal. The infantile phase of the attack had lasted about 30 minutes. She was unable to recall anything that had taken place.

On a subsequent date a similar regression was observed but this time to a level apparently lower than the one just described. Responses to questions were typical of a child between two and three years of age. She was greatly amused with the ticking of a watch. If given other trinkets to play with she would immediately discard them and reach for the watch. She either pitched it up and down as if it were a ball or would hold it to one ear and then to the other to hear it tick. Her smile and behavior gave evidence of her amusement with the new-found toy. The observer threatened to spank her if she did not quit acting like a baby. Her response to this threat was a vigorous cry and pleadings for her mother. This crying spell was followed by a period of complete relaxation and unconsciousness in which she was insensible to all stimulation, even of a very severe nature. She made no reaction to efforts to revive her from

her stuporous and unconscious state. After a few minutes she became partially oriented to her surroundings but was unable to see, hear or talk but was sensitive to stimulation of other parts of the body. Shortly thereafter she began hallucinating. She began talking to someone far off, apparently an angel or God. This period of observation lasted for three hours without the patient being at any time completely oriented and normal.

In other attacks she relived various episodes of her childhood, many of which referred to some unpleasant experience in connection with the cruelty of her mother. At one time she regressed to the age of about nine or ten. She was crying because her mother refused to let her wear a certain preferred dress. She reenacted all the details of humiliation to which she was subjected in

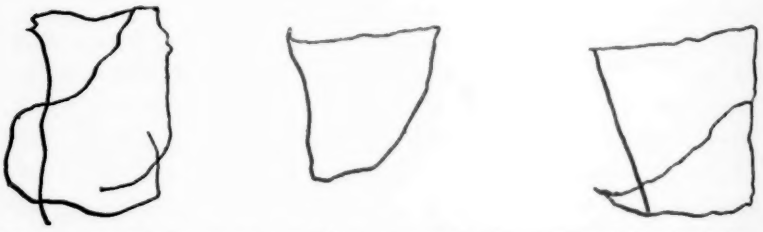


FIG. 1.—Performance on the Binet square at the regressed level of about three years.

front of visiting relatives. When the observer said, "Here is Daddy, what's the matter?" she immediately snuggled into his arms to tell him her troubles. During this attack her aunt and cousin were present and were present also during the original occurrence of the incident. They verified the details of her behavior. On still another occasion, when she had regressed to an age of about eight she wrote out a list of the names of the children in her grade. She was unable to do this in the normal state.

During several of these attacks performances on standardized tests were obtained from her. At one of the infantile levels she endeavored to reproduce the Stanford-Binet square standardized at the four-year level. Fig. 1 shows this response. It is the characteristic performance of the estimated age level. At a regressed level which was estimated to be about eight, she made a satisfactory performance on the triangle standardized at age seven (Fig. 2).

Samples of her writing were obtained at the same time. They also were characteristic of the age.

In order to discover psychic traumas she was occasionally subjected to hypnosis. At successive suggested age levels she was asked to do various performances, one of which was to draw a house. Fig. 3 shows her drawings of a house at each level from age two to age nine. Each house is appropriate for the suggested age and each shows progressive development. In all of the levels to which she regressed without hypnotic influence her writing, drawings, and other objective evidence corresponded approximately to the level estimated by the observer. She also was asked to write her name

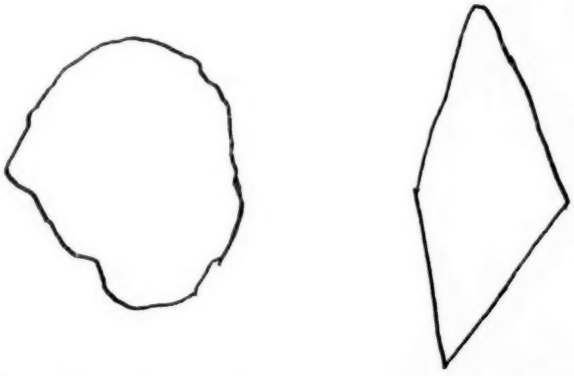


FIG. 2.—Performance on the triangle at the regressed age levels of three and eight respectively.

at various suggested levels from four through twenty. This performance is reproduced in Fig. 4. The quality and speed increased gradually until about 12 or 13. After this level there was no improvement in quality but the speed and facility of the writing movement showed progressive improvement through successive levels. She then was able to write her entire name with greater speed than she was able to make an " M " at the four-year level. At the age of 14 the second part of her name, Ruth, was always added. In all writing or drawing performances she used the left hand through age six and thereafter she used her right hand. Normally she was left handed in all performances except writing.

These and other data were obtained repeatedly during widely separated intervals with consistent results. If this had been a case

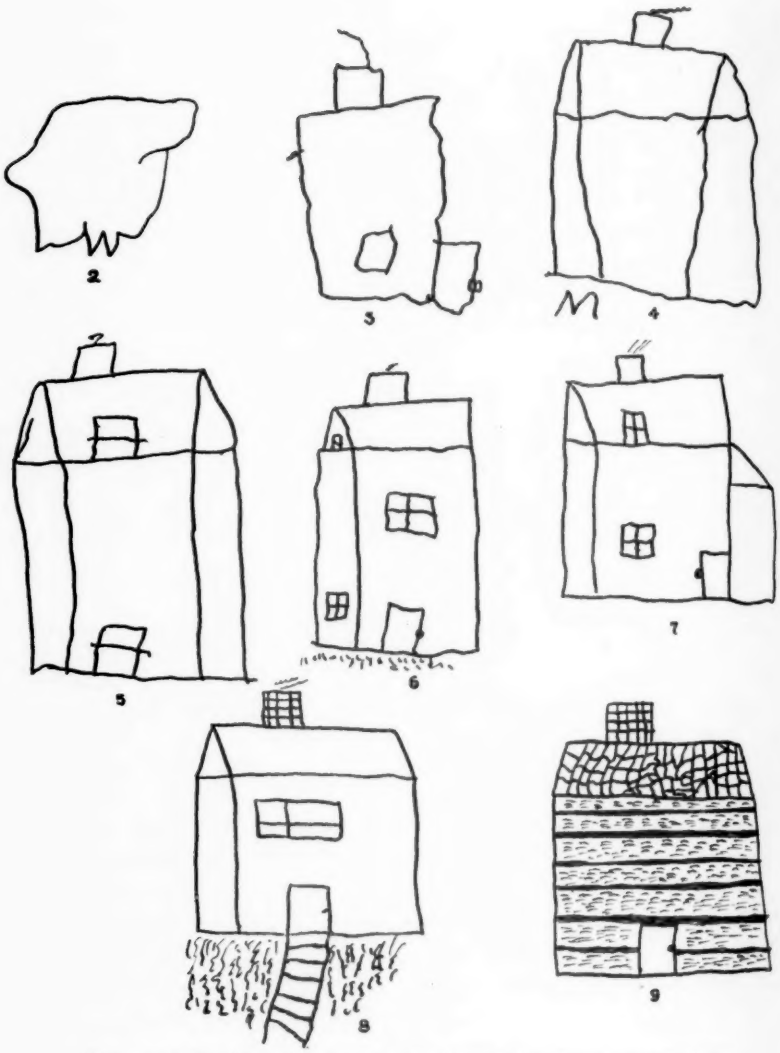
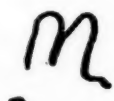
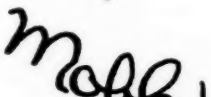
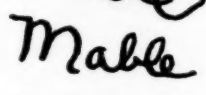
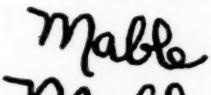
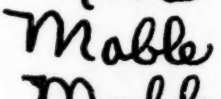
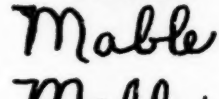
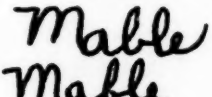
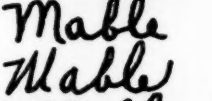


FIG. 3.—Drawing of a house at different levels of regression.

Hand	Age	
L	4	
L	5	
L	6	
R	7	
R	8	
R	9	
R	10	
R	11	
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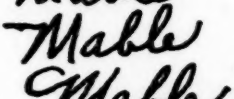
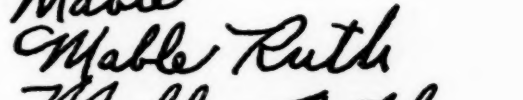
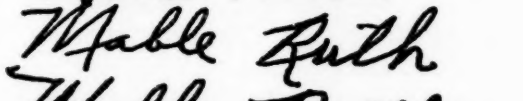
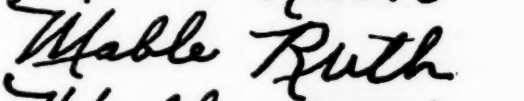
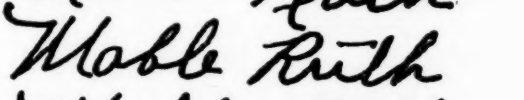
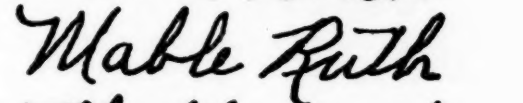
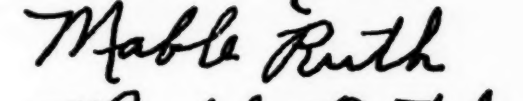
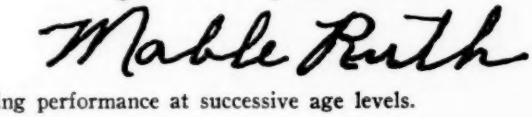
R	13	
R	14	
R	15	
R	16	
R	17	
R	18	
R	19	
R	20	

FIG. 4.—Writing performance at successive age levels.

of malingering she would not have been able to perform so consistently to correspond with the performances of children of these ages. At no time in her normal condition had she seen or heard of a Binet test, was not aware of the performance of children on the square and triangle which she endeavored to reproduce. As a proof of this assumption, several adults who were unfamiliar with the Binet test endeavored to reproduce the Binet square at various assigned levels. In no case was their performance typical of the age level. They invariably over-estimated the performance a child would make. This would seem to indicate, then, that only an individual who had actually regressed to a lower age level is able to perform activities in a way characteristic of the regressed level.

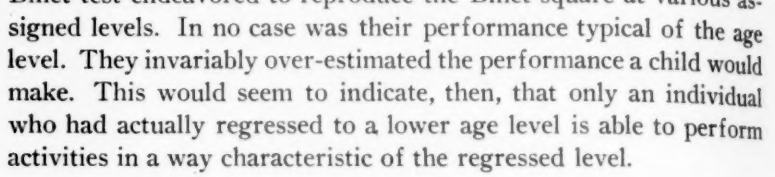


FIG. 5.—Sample of writing performance at age level of about eight.

The treatment consisted in discussion of her troubles and unpleasant childhood experiences and conflicts on a psychological basis. She was shown how these past events and difficulties were the basic causes of her present attacks. She was given semi-scientific but accurate books on hysteria and mental hygiene. She was encouraged to write a history of her life and to describe her attacks and then to give an explanation of them on the basis of the psychological information obtained. Through the assistance of the local newspaper she was able to discover her real parents. She made a satisfactory economic and social adjustment. Within a year after the start of the treatment the patient was apparently normal and well adjusted. The attacks have ceased, she is less impetuous and restless and her former pathological lying has not been observed.

Notes and Comment.

PSYCHIATRIC FILMS.—Dr. Hamilton, Chairman of the Program Committee, submits the following suggestion:

The Committee on Program would be interested to know of films dealing with psychiatric matters. The records made in New York State have already come to the attention of the committee and it is hoped that similar records can be reported in other districts.

Cooperation is invited from all having possession of such films or knowledge of their existence. Correspondence should be addressed to Dr. Samuel W. Hamilton, Bloomingdale Hospital, White Plains, N. Y.

A STANDARD CLASSIFIED NOMENCLATURE OF DISEASE.—A matter of more than passing interest to the members of The American Psychiatric Association is the "Standard Classified Nomenclature of Disease," compiled by the National Conference on Nomenclature of Disease; published recently by The Commonwealth Fund of New York; and edited by H. B. Logie, M. D., C. M.

The following national organizations have approved either the whole Standard Classified Nomenclature, or the section in which each is particularly concerned:

American Medical Association.
American College of Surgeons.
American Hospital Association.
Association of American Physicians.
American Surgical Association.
American Society for Clinical Investigation.
American Public Health Association.
American Statistical Association.
American Association of Obstetricians, Gynecologists and Abdominal Surgeons.
American Dermatological Association.
American Gastro-Enterological Association.
American Gynecological Society.
American Heart Association.
American Laryngological Association.

American Neurological Association.
American Ophthalmological Society.
American Orthopædic Association.
American Psychiatric Association.
American Society of Tropical Medicine.
American Urological Association.
Catholic Hospital Association.
Association of Record Librarians of North America.

It is expected that this nomenclature will eventually be adopted for official use by the U. S. Census Bureau; the Army; the Navy; Marine Hospital Service; Veterans' Bureau; and all of the hospitals—general, special, public and private, in this country. Its use by the administrative departments, boards of control, etc., having to do with mental hospitals, is highly recommended. The classification of psychoses used is that of The American Psychiatric Association with code numbers which correlate the mental diseases with all of the other classified conditions so that they can readily be reported on statistical cards.

REVISION OF THE CONSTITUTION.—In the September 1932 number of the JOURNAL appeared the proposed revision of the Constitution, which will be acted upon at the forthcoming annual meeting. Dr. Earl D. Bond, Chairman of the Committee on Revision, has submitted the subjoined draft which incorporates certain corrections and changes suggested in letters by various members of the Association. In his accompanying letter Dr. Bond states:

I believe that it will be an advantage for the membership to see this revision by itself without the rather confusing parallel articles of the present Constitution.

The opinion of the membership is especially desired upon the word "exclusively" as it appears in Article III, Section IV, and Section V. There have been many suggestions that in Section IV the time of six years should be decreased to five years. It will be noted that in Article VII provision is made for a salaried assistant to the Secretary-Treasurer.

It is the hope of the Committee on Revision and of the Executive Committee that those who wish to suggest any modifications will communicate with the Committee on Revision before the meeting so that as little time as possible will be given to discussion after the revised Constitution is presented to be voted upon. This is because the experience of the committee is that the discussion upon even the minor provisions has tended to be prolonged even in the small committee meetings. Those members who will write to the committee will be sure that their suggestions will be thoughtfully considered and will be brought to the attention of the whole Association.

CONSTITUTION.

ARTICLE I.

NAME.—This corporation, founded in 1844 as The Association of Medical Superintendents of American Institutions for the Insane, known from 1892 to 1921 as The American Medico-Psychological Association and since 1921 as The American Psychiatric Association, is hereby continued under the last designation.

ARTICLE II.

OBJECTS.—The objects of this Association shall be—(A) to further the study of subjects pertaining to the nature, treatment and prevention of mental disorders; (B) to further the interests, the maintenance, and the advancement of standards of hospitals for mental disorders, of out-patient clinics, and of all other agencies concerned with the medical, social and legal aspects of these disorders; (C) to further psychiatric education and research; (D) and to apply psychiatric knowledge to other branches of medicine, to other sciences and to the public welfare.

ARTICLE III.

MEMBERSHIP.—Section I. There shall be six classes of members: Fellows, Members, Associate members, Life Fellows, Honorary members, Corresponding members.

Section II. All classes of membership except Honorary and Corresponding members shall be residents of the United States or its dependencies or British America at the time of their election.

Section III. An Examining Board of five Fellows shall be appointed by the President and approved by the Council. One member of this Board shall retire each year and be ineligible for reappointment. It shall be the duty of this Board to make a report and recommendation to the Council on every application for every class of membership.

It shall also be the duty of this Board immediately after its organization and from time to time afterward to submit to the Council plans for the procedures by which it proposes to pass upon the fitness of new applicants for membership and of present members of the Association, make such other recommendations as it may deem advisable from time to time and perform such other duties

as Council or Association may assign to it. Its plans and recommendations must be approved by the Council.

Section IV. Fellows hereafter shall be chosen from members of not less than one year's standing who have been engaged exclusively in the practise of psychiatry for at least six years.

Section V. Members hereafter shall be chosen from physicians who have been engaged exclusively in the practise of psychiatry for at least three years.

Members shall be recommended to Fellowship as it becomes apparent that they deserve this recognition.

Section VI. Associate members shall be physicians who have had at least one year's practise in a mental hospital.

Section VII. Life Fellows shall be those who have maintained themselves in good standing as Fellows (or formerly as active members) for thirty consecutive years. They have all the rights of Fellows.

Section VIII. Honorary members shall be those who have distinguished themselves by attainments in psychiatry or related sciences or who have rendered signal service in philanthropic efforts to promote the interests of psychiatry and mental hygiene.

Section IX. Corresponding members shall be those who are qualified for Fellowship but who are not residents of the United States or its dependencies or British America.

ARTICLE IV.

OFFICERS.—The officers of the Association shall be a President, President-Elect, Vice-Presidents, a Secretary and a Treasurer whose duties may be combined, and a Council to include the above officers and twelve Fellows of whom the retiring President shall be one.

Vice-Presidents shall be those Fellows elected Chairmen of sections of the Association.

Past-Presidents after their service in the Council shall thereafter be ex-officio members of the Council without the right to vote.

There shall be three Auditors, one of whom shall retire each year.

ARTICLE V.

VOTING PRIVILEGES.—Fellows and Members only shall be entitled to vote at any meeting and Fellows only shall be eligible to

office in the Association. Life Fellows, Honorary members, and Corresponding members shall be exempt from the payment of annual dues to the Association.

ARTICLE VI.

ELECTION OF OFFICERS.—Section I. The officers and four members of the Council and one Auditor shall be elected at each annual meeting. Nominations shall be made to the Association in the order of business at the first session of the second day of the annual meeting by a committee appointed for that purpose by the President during the first month of his incumbency. Elections shall take place immediately. The nominating committee shall consist of five Fellows. It will send out its ballot in the JOURNAL or otherwise, to every member of the Association, at least one month before the annual meeting. Other nominations may be made from the floor.

Section II. The President, President-Elect, Vice-Presidents and Secretary and Treasurer shall hold office for one year. Councillors and Auditors shall serve three years. The President, President-Elect and the four retiring Councillors are ineligible for re-election to their respective offices for one year immediately following their retirement. The President, President-Elect, Secretary and Treasurer, shall enter upon office at the close of business at the annual meeting at which they are elected. Other officers shall enter upon their duties immediately after their election. All officers shall serve until their successors are elected, and qualified.

Section III. A majority of the members of the Council shall constitute a quorum.

ARTICLE VII.

POWERS.—The President shall preside at the annual and special meetings of the Association or Council. In his absence at any time the President-Elect shall act in his place. The President shall appoint committees of the Association.

The President-Elect shall assume the office of President at the close of the annual meeting held one year after his election.

The Secretary shall keep the records of the Association and perform all the duties that may be prescribed for him by the Council. The Treasurer, under the Council, shall receive and disburse and duly account for, all sums of money belonging to the Association;

he shall submit a financial statement each year to the Council at its annual meeting; he shall be placed under bond to an amount which the Council each year directs. The Council may appoint an Executive Assistant or a person otherwise designated on a salary to carry such duties of the Secretary-Treasurer as may be assigned by the Council, having power to receive and deposit moneys for the Association. Such Assistant shall be bonded in an amount to be determined by the Council.

The Auditors shall examine each annual financial statement of the Treasurer and arrange for its audit by certified public accountants. The Auditors will propose and the Council will name the depositories in which the Treasurer shall keep the funds of the Association. The Auditors will act as the Financial Committee of the Council and their recommendations and actions shall be subject to the approval of the Council.

The Council shall control the funds in the possession of the Association. It shall publish a JOURNAL and print annually the proceedings of the meetings. It shall appoint the editor of the AMERICAN JOURNAL OF PSYCHIATRY. It is empowered to appoint Committees from its own membership to expend money for special scientific investigations in matters pertaining to the objects and business of the Association, to publish reports of such investigations, to adopt a budget for current expenses of the Treasurer and Committees for the ensuing year, and to apply the income of special funds to the purposes for which they were intended.

The Council shall elect an executive committee to consist of the President, President-Elect and Secretary and Treasurer with two other of its members which shall have the powers of the Council (at such times as matters important to the Association must be decided and it is considered unnecessary to call the Council together) between meetings of the Council.

The Executive Committee derives all its powers from the Council and the Council derives all its powers from the Association.

ARTICLE VIII.

AMENDMENTS.—Amendments to the Constitution shall be considered at the first session of the second day of any annual meeting and be adopted by a two-thirds vote of all Fellows and Members present and voting: Provided, That notice of proposed amend-

ments has been given in writing at the annual meeting preceding that at which the amendments are submitted for action. It shall be the duty of the Secretary to send to every member, in the JOURNAL or otherwise, at least three months previous to the voting upon an amendment, a copy of its provisions.

Amendments to the By-Laws shall also be considered at the first session of the second day of any annual meeting and may be adopted by a two-thirds vote of all the Fellows and Members present and voting: Provided, That notice of proposed amendments shall have been given to the Secretary and by him published in the JOURNAL or otherwise, at least three months previous to the annual meeting at which they are to be considered, and further Provided, That these amendments have been considered at an appropriate meeting of the Council.

BY-LAWS.

ARTICLE I.

ORDERS OF BUSINESS.—The meetings of the Association shall be held annually, each meeting to extend over at least three days. The place of each meeting shall be named by the Council and reported to the Association for action at the annual meeting preceding. Each annual meeting shall be called by printed announcements sent to each member on its rolls at least three months previous to the meeting, and by publication in the JOURNAL.

On the second day election of officers shall be held and amendments to the Constitution and By-Laws shall be considered.

On the third day elections to the different classes of membership in the Association shall be held. The lists of candidates submitted shall have been passed by the Examining Board and the Council. Before the close of the final session the President, the President-Elect, and the Secretary and Treasurer shall be inducted to office.

The Council shall hold an annual meeting concurrent with the annual meeting of the Association; and shall hold as many sessions and at such times as the business of the Association may require.

The President shall have authority at any time, at his own discretion, to instruct the Secretary to call a special meeting of the Council; and he shall be required to do so upon a request signed by six members of the Council. Such special meetings shall be called by giving at least two weeks' written notice.

ARTICLE II.

Dues.—Each member shall pay to the Treasurer such annual dues and assessments as shall be determined by the Council at its annual meeting.

ARTICLE III.

Resignation and Dismissal.—Any member of the Association may withdraw by signifying his desire to do so in writing to the Secretary: Provided, That he shall have paid all dues to the Association. Any member who shall fail for three successive years to pay dues after special notice by the Treasurer shall be regarded as having resigned membership, unless such payment of dues is waived by the Council for good and sufficient reasons.

The name of any member declared unfit for membership by two-thirds vote of the members of the Council present at an annual meeting of that body, shall be presented by the Council to the Association, from which he shall be dismissed if it be so voted by a number not less than two-thirds of those present at the annual meeting, registered and voting.

ARTICLE IV.

Union with Other Societies.—When another national society with interests similar to those of this Association shall express a wish for an organic union and when this union shall be acceptable to this Association, the following plan shall be adopted:

1. A Section of The American Psychiatric Association shall be established and appropriately named.

2. The medical members of the incoming society who meet the requirements of Article III of the above Constitution, shall become Associate members, Members, or Fellows of The American Psychiatric Association.

3. The other members of the incoming society may remain as members of the Section and shall be placed on a special mailing list but shall not become members of the Association.

4. A section chairman and secretary shall be elected by the section. The Chairman who must be a Fellow, by virtue of his office shall be an Honorary Vice-President of The American Psychiatric Association.

5. The section shall arrange its own program with the co-operation and approval of the Program Committee of the Association.

6. If funds are transferred to the Council of The American Psychiatric Association by the incoming society, the funds shall be devoted to purposes specified or for purposes in accord with the objects of the donating society.

ARTICLE V.

DISTRICT SOCIETIES.—When any state or provincial psychiatric society or a psychiatric society representing a geographical division of the United States or British America shall signify a desire to become a district society of The American Psychiatric Association, and when this shall formally be accepted by this Association, the following plan shall be adopted:

1. The state or local district Society shall be subject to such regulations relating to reorganization and management as may be made by The American Psychiatric Association from time to time.

2. Local organizations shall be allowed to include members who are not eligible for membership in the Association and shall in general be allowed a wide latitude in their organization.

ARTICLE VI.

NEW SECTIONS.—The Council upon its own initiative or upon the application of not less than twenty Fellows or Members, or Associate Members, may present to the Association a proposal for a section which shall have its own special program. Upon approval of the Association the following plan shall be adopted:

1. A section of The American Psychiatric Association shall be established and appropriately named.

2. A section chairman and secretary shall be elected by the section and the chairman shall become Vice-President of the Association.

Association and Hospital Notes and News.

AMERICAN PSYCHOPATHOLOGICAL ASSOCIATION.—The Twenty-third Annual Meeting of the American Psychopathological Association will be held in Washington, D. C., Thursday, May 11. The morning session will be held conjointly with the American Neurological Association, at Hotel Washington, opposite the Treasury Building.

Titles of papers should be in the hands of the Secretary, Dr. L. E. Emerson, 370 Commonwealth Ave., Boston, Mass., not later than April 15.

SIXTY-SECOND ANNUAL MEETING AMERICAN PUBLIC HEALTH ASSOCIATION.—The American Public Health Association, foremost sanitary organization in the United States, announces its Sixty-second Annual Meeting, to be held in Indianapolis, Indiana, October 9-12, 1933.

It was in Indianapolis in 1900 at the Twenty-ninth convention of the American Public Health Association that Dr. Walter Reed read a paper entitled "The Etiology of Yellow Fever—A Preliminary Note" indicating that the mosquito serves as the intermediate host for the parasite of yellow fever. History was being made in the Old German House that day, yet it is reported by some of those present that the epochal report was received with only mild interest.

At the Sixty-second Annual Meeting it is planned to honor the only living participant in the famous Yellow Fever Experiment, Dr. John R. Kissinger, at a special memorial session.

The scientific program will discuss every aspect of modern public health practice, from the viewpoint of the health officer, the laboratory worker, the epidemiologist, the child hygienist, the industrial hygienist, the nurse, the vital statistician, the health educator, the food and nutrition expert, the sanitary engineer. Distinguished scientific pronouncements may be expected from the outstanding personalities in the public health profession who will contribute to the program.

The American Public Health Association, 450 Seventh Avenue, New York City, will be glad to send more complete information about its Indianapolis Annual Meeting, to anyone interested.

THE PSYCHOANALYTIC QUARTERLY.—This new publication has just completed its first year. Under the editorial direction of Drs. Feigenbaum, Lewin, Williams and Zilboorg, the title page presents an international board of collaborators including representatives from Berlin, Vienna, Budapest, Paris, London, Boston, Chicago, New York and Washington. The following original papers appeared in Volume I, which ran to 750 pages:

A. A. Brill: The Sense of Smell in the Neuroses and Psychoses.
Floyd Dell: An Autobiographical Critique.
Helen Deutsch: On Female Homosexuality.
Paul Federn: Ego Feeling in Dreams.
Dorian Feigenbaum: Note on the Theory of Libidinal Types.
Otto Fenichel: Outline of Clinical Psychoanalysis.
J. C. Flügel: Maurice Bedel's "Jerome"—A Study of Contrasting Types.
Sigm. Freud: Libidinal Types.
Sigm. Freud: Concerning the Sexuality of Woman.
Sigm. Freud: The Acquisition of Fire.
Eugen J. Hárnik: Pleasure in Disguise, the Need for Decoration, and the Sense of Beauty.
Abraham Kardiner: The Bio-Analysis of the Epileptic Reaction.
Moses Ralph Kaufman: Some Clinical Data on Ideas of Reference.
Bertram D. Lewin: Analysis and Structure of a Transient Hypomania.
Sándor Radó: The Paths of Natural Science in the Light of Psychoanalysis.
Markus Reiner: Causality and Psychoanalysis.
Géza Róheim: Animism and Religion.
Géza Róheim: Telepathy in a Dream.
Frankwood E. Williams: Is there a Mental Hygiene?

DR. GEORGE A. SMITH'S RETIREMENT.—That well-beloved physician, Dr. George A. Smith, retired from the superintendency of Central Islip State Hospital, December 1, 1932, after 50 years of service. It is given to few men to serve so long, so faithfully and so well, and to have so thoroughly gained the affections of his associates. It is a pleasure to know that these same associates did him honor at the quarterly conference of the New York State Department of Mental Hygiene, held at Central Islip State Hospital, September 27, 1932. The entire afternoon session was devoted to

a review of Dr. Smith's distinguished service in the care of mental patients.

The Commissioner of Mental Hygiene, Dr. Frederick W. Parsons, opened the session and read a letter from Dr. Charles W. Pilgrim, former commissioner and a life-long friend of Dr. Smith. Dr. Parsons then read a tribute, "Dr. Smith's Services to the State," and was followed by Dr. George W. Mills who read a most interesting account, "The Story of Central Islip State Hospital." Brief remarks were made by Dr. Harry P. Robbins, Dr. Jacob Oshlag, Dr. James V. May, President of the American Psychiatric Association, Dr. Robert M. Elliott, Hon. Peter A. Hatting, after which Dr. Richard H. Hutchings, with appropriate remarks, presented Dr. Smith with a watch, suitably inscribed, and Mrs. Smith with a platinum bracelet. The meeting closed with an acknowledgment by Dr. Smith and a eulogy and blessing by Monsignor York.

Dr. Smith was born at Wakefield, New Hampshire, November 9, 1858, and graduated in medicine from Bellevue Medical School in 1881. He entered the New York State Service February 26, 1882, as Assistant Physician at Hart's Island, was promoted to assistant superintendent, and on May 1, 1892, became acting superintendent at the same place. The position known as acting superintendent was really superintendent, but inasmuch as there was a "general superintendent" who was in charge of two or three institutions at one time the administrator of an individual hospital was called acting superintendent.

The JOURNAL wishes to add its felicitations and to wish Doctor and Mrs. Smith much happiness in the less strenuous life they will lead. May they live long and prosper!

APPOINTMENT OF EXECUTIVE ASSISTANT.—After consideration of several candidates, the Executive Committee of the Association, in accordance with resolutions adopted at the Philadelphia meeting, appointed Mr. Austin M. Davies as executive assistant of the Association. Mr. Davies is a graduate of Brown University and during his academic course developed an interest in psychiatry, being associated for a time at the Butler Hospital; his graduate thesis was on the subject of *Mental Hygiene*. After graduation Mr. Davies taught in the Kenilworth schools, Kenilworth, N. J., and for several years was sales representative on new accounts at

the Dollar Savings and Loan Company, Cleveland, Ohio. Subsequently he was Philadelphia sales representative for Babson Statistical Organization of Wellesley Hills, Mass. For the next three years he was education secretary at the Public Charities Association of Pennsylvania. He has latterly been connected with the Lloyd Emergency Relief Committee and Bureau of Unemployment Relief, Philadelphia. He is a brother of Dr. Stanley P. Davies, associate secretary of the State Charities Aid Association of New York, who is well known to many of the members of The American Psychiatric Association.

As executive assistant, Mr. Davies' office will be located with the offices of the National Committee for Mental Hygiene at 450 Seventh Avenue, New York City. Mr. Davies will take over the business affairs of THE AMERICAN JOURNAL OF PSYCHIATRY and will gradually assume the administrative duties previously carried out by the secretary-treasurer.

The Association feels itself fortunate in having been able to obtain the services of Mr. Davies and that through his connection with the Association and with the establishment of a central office in New York City the aims and purposes of the Association will be advanced.

APPOINTMENT OF JAMES V. MAY AS COMMISSIONER OF MENTAL DISEASES IN MASSACHUSETTS.—The vacancy in the position of commissioner of mental diseases in Massachusetts created by the death of George M. Kline has been filled by Governor Ely by the appointment of James V. May, President of The American Psychiatric Association.

Dr. May has had an unusually broad basis of training and wide experience in the administrative problems of the care of mental patients. He has not only had first-hand experience in hospital work but he has also had the responsibility for directing the state-wide care of the insane as Chairman of the New York State Hospital Commission for several years. Since coming to Massachusetts in 1916 he has been superintendent of the Grafton State Hospital and of the Boston State Hospital, from which position he comes to the commissionership.

In addition to his administrative experience Dr. May has shown a continuous interest in problems of clinical nature and has made

valuable contributions to psychiatric literature. Outstanding is his text-book: "Mental Diseases, a Public Health Problem," published in 1922.

In the promotion and organization of mental health activities, Massachusetts has long occupied a position of leadership. Under Dr. May's guidance the maintenance of this enviable position is assured.

SUPPLEMENTARY LIST OF APPLICANTS FOR MEMBERSHIP IN THE AMERICAN PSYCHIATRIC ASSOCIATION:

MEMBERS.

Baker, Asher L., Craig House, Beacon, N. Y.
Barber, Theodore, M., Norfolk, Nebraska.
Chamberlain, Leslie R., Danville, Pa.
Doody, William M., 19 Bentley Ave., Jersey City, N. J.
Douglas, Margaret, Greystone Park, N. J.
Drummond, Clarence C., State Hospital, Norfolk, Nebraska.
Dunbar H. Flanders, 935 Park Avenue, New York, N. Y.
Easton, Norman Lewis, Toronto Psychiatric Hospital, Toronto, Ont., Canada.
Enright, James R., Territorial Hospital, T. H.
King, Frank O., P. O. Box B, Foxboro, Mass.
Kinsman, Edward Homer, Toronto Psychiatric Hospital, Toronto, Ont., Canada.
Jones, Granville L., N. J. State Hospital, Marlboro, N. J.
McKercher, Alexander E., Toronto Psychiatric Hospital, Toronto, Ont., Canada.
Powers, Lillian Delger, 128 W. 59th St., New York, N. Y.
Roeling, George F., 3501 Napoleon Ave., New Orleans, La.
Rothschild, Leonard, 116 W. 59th St., New York, N. Y.
Schwenkenberg, Arthur, 932 Medical Arts Bldg., Dallas, Texas.
Sharpe, John Edward, Toronto Psychiatric Hospital, Toronto, Ont., Canada.
Shellenberger, Edward B., Danville, Pa.
Steen, Patricia, State Hospital, Kings Park, L. I., N. Y.
Steen, Reginald Reed, Kings Park, N. Y.
Stein, Calvert, Drawer F, Palmer, Mass.
Thomas, Jackson M., McLean Hospital, Waverley, Mass.
Wolfe, Theodore P., 935 Park Avenue, New York, N. Y.

Members desiring to comment upon any of these applications will kindly communicate with the Secretary, Dr. Clarence O. Cheney, 722 West 168th St., New York.

Book Reviews.

The Treatment of Behavior Disorders Following Encephalitis. By EARL D. BOND, M. D., and KENNETH E. APPEL, M. D. (*New York: The Commonwealth Fund, Division of Publications, 1931.*)

Here, in simple and untechnical terms, the authors have given us a very illuminating and full account of the treatment possibilities in post-encephalitic behavior disturbances.

Their work is based on the careful long-section study of a special series of 48 cases of both sexes. The procedure followed was essentially the application of close individual attention, on a group basis, along approved child guidance lines and in a hospital setting. The results were striking and, in signal measure, an endorsement of this particular approach. Thus, definite improvement was noted in 46 cases during the period of hospital residence. Among those discharged, interestingly enough, continued good result was observed in 35 percent, a distinctly greater proportion apparently than the reported yield from other methods.

The presentation is developed about eight chapter heads, including in all 163 pages. First there is supplied a very good introduction relative to the nature of epidemic encephalitis as such, and the problems occasioned by it. This orientational section is followed by full discussion of the case series, the therapeutic set-up and the results obtained.

The book is of excellent and attractive format, and stands out as a valuable contribution as to the place of educational and social therapy *per se* in problems basically medical in origin. It is recommended highly to all, both physicians and laymen, who may be interested in the clinical aspects of conduct problems in children.

THEOPHILE RAPHAEL.

Personal Hygiene for Nurses. By SENECA EGBERT, M. D. (*Philadelphia: F. A. Davis Company, 1930.*)

Dr. Egbert, Professor of Hygiene at the University of Pennsylvania, in this neat 350-page volume, makes a really very good addition to the group of texts on personal or individual hygiene for nurses.

In this book, the author covers the whole broad field of hygiene, simply yet adequately and scientifically, and the presentation is well within the grasp of pupil nurses. The treatment is nicely rounded out, biologic, anatomic, physiologic, psychologic, pathologic and sociologic facts and implications being very properly stressed, and integrated into a unified whole, *i. e.*, the functioning human organism. Also, as a text, the arrangement is excellent, with well organized chapters helpfully broken up by frequent section and

subsection heads. The work is well illustrated, with short bibliographies and review questions following each chapter. At the end of the volume is appended an additional bibliography and, likewise, a good index.

As to psychiatric or mental hygiene material, while allusions occur here and there through the book as a whole, this particular aspect is specifically treated in the 10th chapter, which deals also with the structure and function of the nervous system. The specific topics here discussed, it might be mentioned, are mentality, habits, tension and fatigue, rest, sleep and recreation.

THEOPHILE RAPHAEL.

Social Control of the Mentally Deficient. By STANLEY P. DAVIES. (*New York: Thomas Y. Crowell Company, 1930.*)

This second edition of Dr. Davies' work of 1923, needs no special introduction. Much expanded and reworked and brought thoroughly up-to-date, it stands out, even more than originally, as a classic synthesis in the field, and is highly recommended to all interested in the general problem of mental deficiency.

In its present form (389 pages), the volume comprises 18 chapters, very simply written but comprehensive, dealing with the various aspects of the question, historical, factual and practical, technical, sociologic and therapeutic. Likewise, among other uses, because of its directness and crystallinity of organization, it lends itself excellently for text-book purposes. Representative and as of especial interest might be mentioned the following sections—The Social Test of Mentality, An Invention and a Discovery (dealing with the coming of psychometry), Eugenic Alarms, The Social Indictment, Sterilization, Changing Concepts of Heredity, Newer Aspects of Behavior, The Institution as a Socializing Force, Community Supervision, and The Mentally Deficient in the Social Order.

The author takes a gratifying balanced and pragmatic and non-extremist point of view, harmonizing and evaluating differing attitudes and opinions, as for example with respect to sterilization. His approach is not in any way a single or isolated one; rather, it is as complete as possible a presentation of the entire situation, and from all angles. In other words, we have emergent the mental defective as a human being, a functional element of the social mass, a living part of the social process. This seems to the reviewer the only rational envisagement and procedure, if this complex problem is to be furthered in its understanding and handling.

THEOPHILE RAPHAEL.

The Mechanism of Nervous Action. Electrical Studies of the Neurone. By E. D. ADRIAN. (*Philadelphia: Univ. of Penn. Press, 1932.*)

Being the second series of lectures on the Eldrige Reeves Johnson Foundation, given by the Professor of Physiology at Cambridge University and, for the most part, as an account of work for which the author later was crowned a Noble Laureate, these lectures are authoritative simply as a foregone conclusion. But that they are done with a beauty of style rarely

equalled in physiological literature is a matter which can be appreciated only by a perusal of the text. Admirably avoiding needless use of technical terms in this most technical of technical fields, combining brevity with clarity, swiftness with sureness, the author states the problem, describes the newfound keys for its solution and the quarry thereby and thus far unearthed. Here and there the general reader is given a plum in the form of a very cautious hint as to the significance of the new findings in the whole framework of nervous action.

Physiologists and neurologists interested in knowing what the contributions of Adrian and his associates have been to the modern trends of electrophysiology will find in this book a splendid résumé. The psychologist and the psychiatrist should not be deterred from its study by the undramatic conclusion that the reactions of specialized cells of the nervous system "do not differ fundamentally from one another or from the reactions of other kinds of excitable cell. They have a fairly simple mechanism when we treat them as individuals: their behavior in the mass may be quite another story, but this is for the future to decide."

CHARLES D. SNYDER,
The Johns Hopkins School of Medicine.

Sur l'activité spontanée normal et pathologique. By ABRAHAM BARNETT. (*Paris: 1931.*)

From the earliest times it has been observed that the two chief incentives to activity on the part of man and animals are hunger and sexual desire. Likewise has it been observed generally that sexual desires are apt to rise in the well fed, to subside during starvation, and that if for any reason an animal is "off his food" then not only the search for food abates but also the search for mates. In brief, bodily activities go along with the visceral.

In spite of these self-evident facts psychologists in recent years have thought the matter worthy of being put to purely objective, experimental proof, which apparently they had no trouble whatever in doing.

It is this scientific work that Dr. Barnett reviews and uses as a point of departure, classifying thereupon all normal activities either as spontaneous, or forced (provoquée); that is, into those activities that seem to arise from inner stimuli and even to send the subject out in search of stimuli, and those that must always be provoked, occurring only in response to such external agents as happen to come along. The rôle of the internal secretions is discussed in relation to the spontaneous activities, which latter are then subdivided into the two elemental drives mentioned above and a third, the social, which reach their highest development in man, and which arise from a cultivated sense of self-esteem and an urge to receive the approbation of one's fellow.

Psychopaths are viewed as abnormal in these classes of activities, and accordingly may be divided into (1) hyperactives, maniacs, (2) hypoactives, melancholics, (3) dysactives, those exhibiting schizoid and paranoic syndromes and those amenable to psychotherapy. The problem in the treatment of all types is to bring them back to a normal level of spontaneous activity. And

since it is shown that the bodily activity is determined by the visceral, the hyperactives are to be well fed, drugs given to quiet the gut (papaverine, benzyl-benzoate), and gonad activity reduced with x-rays or by complete removal. The hypoactives on the other hand, should have their meals spaced farther apart, given drugs to increase vagal tone, and phosphates; folliculin injections are to be given both sexes. The dysactives are to be treated by psychoanalysis or by other forms of psychotherapy capable of engendering an attitude of self-confidence which will hold spontaneous activity to its normal level. Although in principle this therapy has been in use for many years perhaps the present author's analysis will be illuminating to the student. Experience will teach one much as to the short-comings of the specifics which the author mentions, but the principle may well be adhered to in trying out more effective and less harmful ones.

CHARLES D. SNYDER,
The Johns Hopkins School of Medicine.

Children's Behavior Problems. By LUTON ACKERSON. (*Chicago: The University of Chicago Press, 1931.*)

This is a first monograph in a projected statistical study based upon the examination of 5000 children at the Illinois Institute for Juvenile Research. The data were obtained from the clinic files. The aim of the study in general is to evaluate the causal factors in behavior difficulties of children. The records were examined with special reference to behavior difficulties and reasons for referring. In this volume are shown the efforts to fix upon a series of categories among children's behavior problems, and their incidence, as ascertained from a large group referred to a behavior clinic, and to ascertain the relation of personality and conduct problems to chronological age and to intellectual level. Comparative frequencies of specific behavior difficulties are shown for white girls, white boys, colored girls, and colored boys. The problems are further grouped into conduct and personality categories. There can be no question but that background information of this sort is essential for our better understanding of the probable importance for prognosis of the occurrence of certain types of problems at certain ages. It would seem that an equally large control group of children who have never been referred to clinics could be subjected to a similar study, throwing even further light upon the whole question of the incidence of conduct and personality problems in children.

ALICE J. ROCKWELL, PH. D.,
Baltimore Mental Hygiene Clinic.

Mental Measurement of Pre-School Children. By RACHEL STUTSMAN. (*New York: World Book Company, Yonkers-on-Hudson, 1931.*)

After chapters on the importance, history, and criteria of selection of mental test scales for young children, Dr. Stutsman offers a full report of the Merrill-Palmer research on tests for pre-school children. A section of the book is devoted to the presentation, description, and guide for administer-

ing the Merrill-Palmer Scale, a scale which in its earlier form was presented by Miss Stutsman as "Performance Tests for Children of Pre-School Age" in Genetic Psychology Monographs, Vol. 1, No. 1, (1926). In its early form this test material had already demonstrated its value and was widely used in clinics. The present volume fills a real need, as the wide acceptance of the tests has already indicated. The test material is peculiarly suited to gain the cooperation of young children, and the directions for administering, scoring, and interpreting the material are exceedingly well presented. It is not a scale which is suitable for administration by other than trained examiners, as it contains 93 separate items to be scored and is best used by examiners who have made a careful study of the scale, who have complete familiarity with all the materials, and who are adept at working with very young children.

ALICE J. ROCKWELL, PH. D.,
Baltimore Mental Hygiene Clinic.

A Point Scale of Performance Tests. By GRACE ARTHUR. (*New York: Division of Publications, The Commonwealth Fund, 1930.*)

This scale was developed in response to a need for a performance scale for general use in clinical work. It has long been recognized that the inclusion of performance (non-verbal) tests in psychological examination is of vital importance in getting a truer picture of the individual's ability. Miss Arthur presents a scale which has been so carefully standardized that the clinician may have confidence in the results. The tests used are those already familiar in psychological clinics throughout the country. This book is written as a clinical manual.

ALICE J. ROCKWELL, PH. D.,
Baltimore Mental Hygiene Clinic.

Juvenile Delinquency. By WALTER C. RECKLESS and MAPHEUS SMITH. (*New York: McGraw-Hill Book Company, 1932.*)

Within 12 chapters the authors give logically and precisely a thorough study of juvenile delinquency presenting case material, statistical data, and the results of the work of various psychiatrists, psychologists, and sociologists whose opinions in this field have come to be considered as authoritative.

The newer conception of juvenile delinquency is portrayed thus, "The offending child is in conflict with the behavior codes of the normal home, school, neighborhood, and community. We call him unadjusted or maladjusted, because his behavior is out of harmony with the standards of chastity, property, order, and personal safety with which we are familiar and to which we yield our social approval." Varieties of maladjustment are outlined from Thomas and Thomas, "The Child in America" in a rather complete classification. "It is beginning to be realized that delinquent children are pretty much the same as other children." Reference to Burt and Healy supports this view. The chief sources of numerical data of juvenile offenders are those of institutional population. In 1928 there are said to have

been 200,000 juvenile offenders in the United States. "Delinquency is not an attribute to any one age, sex, race or nationality group." There is difficulty in obtaining statistics on offences through a lack of uniformity in the definition of delinquency. Among the methods of disposition of delinquent cases, dismissal, probation, and commitment to institution are most common. An interesting quotation is given from Healy, Bronner, *et al.*, "The otherwise normal child who has acquired antisocial habits owing to a lack of parental control, desire for excitement, etc., has an excellent chance of having his behavior reconstructed into that of a useful citizen." The discussion of physical and mental traits leads to a critical evaluation of the methods employed by Goring, Lange, and others who dealt with heredity as a factor in crime. The relationship of physical factors, physical defects and delinquency is rather fully discussed as is also association of delinquency and mental defect.

"Critical analysis and scientifically controlled study have shown the relative and tentative nature of all single factor explanations of delinquency. The same thing may be said of groups of factors, such as, home influences, school influences, the influences of companions, the influence of street environment, and so on. The fact always remains that no group of factors will explain every case unless what is meant is the total personality as composed of its factors." The discussion of truancy and school maladjustment is along the line of causation and prevention. The general study of clinical causation of juvenile delinquency is a most interesting chapter. By a comparison of Healy's 823 Chicago cases and Cyril Burt's study in England the existence of major and minor causal factors is clear. No one factor alone is the cause of delinquency, and the accepted modern procedure is to search for particular factors.

The Juvenile Court is discussed in a most interesting way, showing the development of the movement, its present extent, jurisdiction, organization, and standards and methods of procedure. Institutional versus individual treatment receives careful attention. "One of the greatest handicaps of the reformatory and correctional school form of treatment is that the children when discharged return to the old environment. Returning the child to the former environment assumes that the trouble was with the child and that the reformatory has corrected the badness. But the trouble may be with the family situation, and the child even though reformed, may easily slip back into the behavior of the former type." The narration of institutional experiences by individual boys, such as "The Jack Roller" by Clifford R. Shaw, brings out in clear relief the facts of mass treatment, rigid discipline, beginning of antisocial attitudes, and the taking over of the "code." Just how far the institutions at their present level of development can reach in actually correcting and readjusting with child personality cannot be estimated." The institutional program has most trouble with restless, discontended, sensitive types, and it cannot insure permanent correction.

The development of psychiatric hospitals in America, of the mental hygiene movement, and of child-guidance clinics, is traced. In 1928, there were 490

clinics for child-guidance work in 348 communities in the United States. The organization and methods of the child-guidance clinics are described. "The psychiatric approach has not given the results its most enthusiastic supporters insisted it would. It has fallen heir to many doubtful psychoanalytic conceptions of behavior tendencies and mental processes, and has become somewhat overinterpretive of data obtained from interviews and social histories."

Foster home placing as practiced in Massachusetts has the weight of evidence of 501 actual cases in which the Judge Baker Foundation, cooperating with private child-placing agencies, the probation department of the Boston Juvenile Court, and the State Division of child guardianship, made an effort "to discover the possibilities of foster home treatment of children and adolescents who present problems of misconduct or exhibit undesirable habits or personality characteristics." Non-delinquent children of normal mentality were 95% successful and delinquent children of normal mentality were 85% successful in adjustment by the foster home program. Various other preventive programs are described, even up to the more recent habit clinics for children of the pre-school age, nursery schools and parent education. The results of treatment by various methods are handled quite objectively and a real effort is made to get at facts.

In a study of this kind it is impossible to overlook the pioneer work of Dr. William Healy and his colleagues. The authors have referred to several of the writings of Dr. Healy and his co-authors with striking effect, notably in regard to the value of foster homes to adjust difficult behavior.

While the statistical data refer, of course, to the United States, the material is of interest to students in other countries and some instances may set up a challenge for comparison.

Four appendices are added dealing with individual case studies.

The workmanship is of a high quality, and we have failed to notice a single typographical error.

The book is heartily recommended to any student of juvenile delinquency on account of the scope of its inquiry, the authoritative value of the facts it presents, the pertinent discussion of the views of other competent workers, and the interesting arrangement of material.

E. P. Lewis,
Toronto Psychiatric Hospital.

Personality, Many in One. By J. W. Bridges. (*Boston: The Stratford Company, 1932, pp. 215.*)

Personality, Many in One is a presentation of the concepts of elementary psychology in a simple and lucid style. The author has shown the development of these concepts as they are related to the major topics discussed, *i. e.*, personality, character and temperament. These topics have been treated without bias and although no especially new points of view are set forth, sufficient historical and contemporary literature has been cited to make the book worthy of perusal by psychiatrists and psychologists. One topic is handled in a way

that is different from the usual academic treatment. Bridges' manifold conception of intelligence does not follow the usual prescription. Intelligence is considered from the affective, cognitive, conative and motor points of view. The distinguishing of four types of intellect rather than four components of the intellectual process may lead to some confusion on the part of the lay reader. On the whole, the author has achieved his aim with success and the book will be found especially useful in enabling the non-professional reader to form a clear understanding of the general principles of psychology as well as personality.

ROY M. DORCUS,
Johns Hopkins University.

Statistical Analysis of American Divorce. BY ALFRED CAHEN, PH. D. (*New York: Columbia Univ. Press; London: P. S. King & Son Ltd., 1932.*)

This concise volume of 150 pages is number 360 of the studies in History, Economics and Public Law, edited by the Faculty of Political Science of Columbia University. It constitutes "the only current statistical survey of the United States Census divorce records from the Civil War to the present time."

The author's calculations show that about 18 per cent of all American marriages end definitely in divorce. The number of divorces granted in 1929 was 201,468. To these must be added the desertions, which cannot be accurately determined, but which are estimated conservatively at 50,000 annually. During the 63 year period under consideration the increase in the divorce rate was fivefold. It is a striking and suggestive fact that despite annual fluctuations the divorce rate "has increased very uniformly every decade from the Civil War to the present time." In 1870 only 6 states (Washington, Oregon, Nevada, Wyoming, and let it be noted, blue-law Connecticut and Rhode Island) reported divorces to the number of 75 or more per 100,000 population. By 1900, 31 states fell into this category. In 1929 only 4 states (New York, North Carolina, South Carolina—the only state with no divorce law—and Georgia) showed a divorce rate of less than 75 per 100,000 population.

The author casts a mathematical glance ahead and suggests that if the present rate of increase year by year continues, the year 1965 "would show about 51 per cent of American marriages ending in divorce."

The relative frequency of divorce increases geographically as one journeys across the continent from East to West, the rate for the Pacific coast states being three times as high as that on the Atlantic seaboard. "Portland (Oregon) for many years has been the highest divorce producing city among localities of over 100,000 population in this country, averaging more than one divorce for every two marriages."

It has been proposed that a single federal divorce law should replace the present 49 varying statutes. The author deals thoughtfully with this proposal "strenuously advocated by well-intentioned but misinformed people," and points out the danger of political meddling in complex social problems which

present such widely divergent aspects in different parts of the country. "A federal divorce law would deprive the country of 48 experimental laboratories in social legislation, which provide the primary sources of improvement. Every year a few states modify their divorce laws, several dozen legal changes occurring every decade. Divorce in America is still a flexible and changing problem, unready for a standardized legal solution. . . . . The District of Columbia, granting divorce only on the ground of adultery, is an example of congressional legislation. On this basis, should one wish to intrust Congress with the moral affairs of the American family?

"Trends of the Vanishing Family" is the subject of one chapter. As might be expected there is relationship between the number of children and the likelihood of divorce. Nearly two-thirds of divorces are obtained by childless couples; another fifth by parents with only one child. The author shows that "71 per cent of childless marriages in America end in divorce, while 8 per cent of married couples with children eventually are divorced." An interesting computation shows that the highest number of divorces occurs in the third year of married life, and that the average duration of marriages destined to end in divorce is about seven years. Significant also is the increasing tendency to seek divorce during the early years of married life. There is a progressive shortening of married life of families ending in divorce.

Among the factors in the fivefold increase in the divorce rate during the past six decades the author cites the greater distribution of wealth, urbanization, the changed status of women, the declining birth rate, progressive liberalization of mores with growing social approval of divorce, and finally the steady decline of religious influence. It is one of the effects of advancing civilization.

As the author explains this study is essentially a quantitative one. It makes no pretence to furnish the psychology of divorce. Wholesomely it avoids all moralizing; it does not even "view with alarm." It has valuable data for the sociologist, the psychiatrist and the mental hygienist, for it sets out the metes and bounds of a national habit which figures now in the etiology, again in the symptomatology, and not infrequently in the therapy of mental disorders.

C. B. F.

Foundations of Abnormal Psychology. By FRED A. MOSS, PH. D., M. D., and THELMA HUNT, PH. D. (*New York: Prentice-Hall, Inc., 1932.*)

This work is frankly a text-book of psychiatry and it seems unfortunate that it is not so named. The rather monstrous binomial "abnormal psychology" is only another way of saying "psychopathology" and is therefore an unnecessary term. Moreover, it may mislead the clinician or student who is looking for an exposition of the nature of mental disorders and their treatment. The table of contents however, sets us right. Here we find the traditional pattern of psychiatric hand-books—a general section setting forth the physical basis of mind, the relativity of normal and abnormal, an his-

torical résumé, the prevalence and social and economic significance of mental disabilities, their causes, symptoms, methods of study, treatment and prophylaxis; and a special section dealing with classification schemes and discussion of the major disease types. The authors' classification is etiological.

The guiding principle of this book is in sharp contrast with that of another well-known treatise, also originating in Washington, D. C., namely White's *Outlines of Psychiatry*. The authors of both works have been on the faculty of George Washington University and consulting psychiatrists at the Gallinger Municipal Hospital; but they approach their subject from opposing standpoints. White gives ample scope to the principle of psychogenesis, with a definitely Freudian orientation; Moss and Hunt are avowedly materialistic, even mechanistic. They recognize only bodily causes of mental disturbances. "It is a thesis of this book," they declare in their opening chapter, "that so-called 'mental' factors do not cause disease (either physical or mental) except through their physiological effects." But with that qualifying phrase the proponent of psychogenesis would hardly quarrel. Again: "Mental disorders are to be defined just as other diseases are defined, as pathological conditions resulting from certain bodily disturbances." That sounds more rigid; and when the authors continue that "hallucinations and delusions of those suffering from mental disorders are just as natural outcomes of the underlying bodily condition, as the symptoms of typhoid fever are the outcome of bacterial action in the digestive tract," we recognize the goal that the last two or three generations of tissue pathologists have been aiming at but so far, unhappily, not hit. We can only wish that evidence might be adduced that the statement is true. It would tremendously simplify the subject of mental disease.

The clinical section of the book follows consistently the principle above enunciated. Mental diseases are dealt with in the following order: (1) Those due to bacterial infection—syphilitic psychoses, encephalitis, etc. (2) Intoxications, both exogenous and endogenous. "Exhaustion psychoses" are retained as an example of mental disorder due to endogenous toxins. (3) Endocrinopathies. (4) Conditions caused by deficiencies in cell nutrients. Here are classified pellagra, "some cases of epilepsy," (those responding to dietary treatment), catatonic dementia præcox (because of results reported from carbon dioxide-oxygen treatment), and disorders due to deficiencies in red blood cells (anæmias). (5) Conditions resulting from nerve cell deficiency, notably feeblemindedness. The authors cite here also a variety of psychoses and neuroses in which they believe nerve cell deficiency "undoubtedly constitutes a common factor." They quote with apparent approval such dogmatic generalizations of R. J. A. Berry as the following: "Were a systematic microscopic examination made of the cortical cells of all patients who have died after having suffered from many of the neuroses and the so-called psychoneuroses, it is very probable that amentia would be found to be the common underlying physical factor." (6) Disorders due to brain atrophy, arteriosclerosis and other senile changes. (7) Disorders due to developmental or mechanical injury to brain tissue (microcephalus, hydrocephalus, birth injuries, traumas of later life, brain tumor, hæmorrhage, etc). (8) Disorders

resulting from temperature disturbances (febrile psychoses, sunstroke, the lethargy of low temperatures). (9) "Mental disorders the causes of which are only partly known" (epilepsy, dementia præcox, manic-depressive psychoses, neurasthenia). (10) "Mental disorders the causes of which are unknown" (paranoia, hysteria, psychasthenia). By "causes" under the last two headings it must be remembered definite physical conditions are meant. The authors discuss the etiology of these disorders notwithstanding.

It is a refreshing book, with an uncommon literary flavor. The psychiatry of Shakespeare is amply credited; senile dementia is illustrated, for example, by a seven page discussion of King Lear, with symptoms presented by quotations from the tragedy. One cannot but admire the authors' idealism, if we may call it that, in their staunch adherence to the thesis of tissue pathology for every type of psychic disturbance; and it may be regarded as orthodox medical doctrine by which students should begin their study of psychiatry. As for Freudian hypotheses Moss and Hunt will have none of them. They devote a chapter of 13 pages to an exposition of phychoanalysis and a cutting criticism of its theories and assumptions. They damn Freudian metapsychology, not with faint praise, but thoroughly.

But for the psychological interpretation of symptoms or for psychopathology as such one will look in vain in this book. At best it is a hard and mechanical psychology, in which the emotions are the unwanted children. The pathogenesis of mental states is hardly mentioned; and the subject of mental examination is dismissed with a brief discussion of intelligence tests and tests of personality traits.

The treatment section is inadequate. The measures outlined refer wholly to the physical status. There is no mention of psychotherapy anywhere in the book, and the word does not occur in the index. The nearest approach is in a two-page section on reëducation, which deals however with muscle training and speech disorders, with a single paragraph, like an afterthought, to the effect that "reëducation is also of value in treating the mental side of nervous diseases."

As a brief elementary treatise presenting mainly the physical aspect of psychiatric conditions, the book is an excellent introduction to the study of mental disease and is certainly to be preferred to those works which reflect the tendency to take leave of the physical and to take flight into the metaphysical. The student making use of the present work however, would need to supplement it with a good text on psychopathology.

C. B. F.

In Memoriam.

GEORGE M. KLINE, A. M., M. D.

The Commonwealth of Massachusetts lost a very distinguished servant, and the medical profession in the United States sustained a very severe loss by the death of George M. Kline, Commissioner of the Department of Mental Diseases, which occurred in Boston, January 5, 1933, after a short illness.

Dr. Kline was born in Pittsburgh, Pennsylvania, on March 6, 1878. After being educated in the public schools at Grand Rapids, Michigan, he proceeded to the Medical School of the University of Michigan where he received the degree of M. D. in 1901.

From the date of his graduation Dr. Kline devoted himself to the specialty of psychiatry. His first year was spent as assistant physician at the Worcester (Mass.) State Hospital where he had the stimulus of the teaching of Dr. Adolf Meyer. The next four years were spent as assistant physician at Mt. Pleasant (Iowa) State Hospital, after which he spent six years as first assistant physician at the State Psychopathic Hospital of the University of Michigan, Ann Arbor, Michigan. From this position he was appointed in 1912 superintendent of the Danvers State Hospital, Hathorne, Mass. The administrative ability demonstrated in this position led to his appointment in 1916 as director of the new Massachusetts Commission on Mental Diseases. When the commission was reorganized in 1919 and became the Department of Mental Diseases Dr. Kline was appointed commissioner. He held this position continuously from 1919 until the time of his death, and throughout the whole of this period he devoted himself in a whole-hearted way and with all the resources of his energetic disposition to the duties of his office.

Dr. Kline had not only the grasp of detail which enabled him to be a successful superintendent of a hospital, he had also breadth of vision, imagination, practical judgment, ability to deal with men, and the force of character which enabled him to put into execution

schemes, which a less vigorous personality might have left as a theoretical ideal.

His executive gifts and organizing ability led him to make out of a group of more or less isolated hospitals a state system functioning as a unit, adapted to the special needs and resources of the commonwealth.

Among the many practical measures which he instituted for the efficient functioning of this system, one may mention the standardization of records at all institutions, the adoption of uniform rules and regulations, the adoption of a ration allowance for determining the food requirements at the various institutions, the establishing of a printing plant at the Gardner State Colony to serve the needs of the department and its various hospitals.

To see that the detailed operations within this system should be efficiently carried out, he created such positions as that of farm investigator and assistant engineer.

In many states there is no sound policy for dealing with the annual increase of the number of patients who require hospital care, with the result that from time to time there is apt to be a frenzied and frequently inadequate building program. Dr. Kline looked into the future, studied carefully and statistically the probable rate of growth of the demands on the hospital system, and, on the basis of the best data available, he outlined a careful ten year program of construction.

It would, however, be doing an injustice to the memory of Dr. Kline if one were to put problems of administration in the foreground. His most earnest ambition was that the sick patients under the charge of the Department of Mental Diseases in Massachusetts should have at their disposal the best medical and nursing attention and the best facilities which the commonwealth could supply. He was, therefore, interested in all measures which might be taken in order to keep the standard medical care as high as possible. He established a uniform curriculum in the training schools for nurses in the institutions under his department, he created the position of director of social service work throughout these hospitals.

The trend of medical thought of late years has been very strongly in the direction of preventive work, and Dr. Kline was one of those who most strongly emphasized and cordially advocated the desirability of devoting adequate time and effort to prevention. Interested

as he was in making available to the patients under his department all modern methods and facilities for treatment, he realized that for the public welfare more is to be hoped for from sound preventive work than from the care of those who have suffered disaster. The state hospitals in the past have remained somewhat isolated from the general health facilities of the community. Dr. Kline devoted a great deal of his interest to the organization of out-patient clinics in various cities and towns, not merely clinics where discharged patients might keep in touch with the hospital physicians, but where patients at the very earliest stage of a nervous or mental disorder might go to get advice, thereby possibly avoiding the necessity of a later admission to a state hospital. Special clinics were also established for children, as it was recognized that it is in childhood that habits are formed, emotional values are established, faulty attitudes towards the family and society may become ingrained.

Within the last twenty years the rôle which mental defect plays in a community has been more clearly realized. Dr. Kline saw that a state program should involve a great deal more than merely providing institutional care and training for those mentally retarded children, whose needs are so urgent that they cannot be looked after in the community. He therefore took an active part in outlining a program which would include the early diagnosis of all mentally retarded children, their registration, their education and supervision and the segregation of those not able to be assimilated by the community.

The Department of Mental Disease, cooperating with the Department of Education, was given authority by the legislature to take steps to establish traveling clinics which would give effect to the general program.

With the same broad perspective which was at the basis of this program for the mentally retarded, Dr. Kline cooperated in outlining a program which would do justice to those vulnerable individuals who, by virtue of their mental constitution, should have fallen into the hands of the law. He gave his support to the special legislation known as the "Briggs Law" which gave effect to this program, and he accepted the responsibility for carrying out the examination of certain groups of accused prisoners under the auspices of his department. In a similar spirit he supported legislation which gave the department the responsibility for seeing that

all juvenile delinquents should receive an adequate examination of their mental condition before being committed to a state authority for training or supervision.

A review of these accomplishments gives some idea of the scope of Dr. Kline's work and of the progressive nature of his administration. As his interest in preventive work over-shadowed his interest in the administrative problems of custodial care and medical treatment, so his progressive outlook made him lay a great deal of stress upon further research into the basal conditions underlying mental disorders and not merely upon the application of the knowledge already available. He therefore supported special pieces of research at certain of the state hospitals, research into problems of the greatest importance to the community, such as epilepsy, neurosyphilis, dementia præcox, heredity, the effect of various drugs upon the general working of the central nervous system.

Not only was the ability of Dr. Kline recognized by his immediate associates and by the authorities of the Commonwealth of Massachusetts, but throughout the whole of the United States his services were in wide demand. In 1924 he assisted the Department of Public Welfare of the City of St. Louis to plan their future buildings. In the same year, after making a survey at the request of the Governor of Texas, he brought in recommendations which were later made the basis of legislative measures. In 1929 he carried out a survey for the Governor of Arkansas, and in the same year he gave the benefit of his experience to the State Conference on Mental Health held in Indianapolis. Over a period of years his advice was frequently sought and gratefully accepted by those responsible for the care of the insane in the Province of Quebec, Canada, and in 1929 in recognition of the value of his advice the French Government made him a Knight of the Legion of Honor.

Dr. Kline was a member of many professional associations related to his own branch of medicine. The American Psychiatric Association elected him president in 1926-27; a photograph of Dr. Kline at the time of his presidential address appeared in THE AMERICAN JOURNAL OF PSYCHIATRY for July, 1927. He was also president of the Massachusetts Psychiatric Society (1925-26), and at the time of his death he was president of the New England Society of Psychiatry. As a member of the Scientific Administration Committee of the National Committee for Mental Hygiene his advice

was highly valued. He was a member of the Committee on Organization of the First International Congress of Mental Hygiene (1930). He was a member of the Medical Council of the United States Veterans' Bureau (now a part of the Veterans' Administration) since its creation in 1924. During the World War Dr. Kline gave his services on various advisory bodies dealing with the special problems related to his field.

On June 22, 1931, his Alma Mater conferred on him an honorary degree (M. A.) and expressed its high appreciation of his accomplishments.

On June 23, 1906, Dr. Kline married Ethel A. Fry of Grand Rapids, Michigan, and had two daughters. In private life Dr. Kline was a man of simple tastes and of genial disposition, a loyal friend, highly respected by his colleagues and by all with whom he came in contact. The sympathy of all his friends goes out to his family in their tragic loss. His memory will continue to exert a powerful influence for good on the social welfare of the Commonwealth of Massachusetts, his achievements will be a stimulus to those who come after him.

C. MACFIE CAMPBELL.